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(54) Title: T-TYPE VOLTAGE-GATED CALCIUM CHANNELS AND METHOD OF USING SAME**(57) Abstract**

The present invention provides an isolated or substantially purified nucleic acid encoding a protein comprising at least one domain of a T-type calcium channel and cells and cell lines expressing such nucleic acids. The present invention also provides an isolated or substantially purified T-type calcium channel and an isolated or substantially purified antibody molecule recognizing an epitope on a T-type calcium channel protein.

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T-TYPE VOLTAGE-GATED CALCIUM CHANNELS AND METHOD OF USING SAME

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TECHNICAL FIELD OF THE INVENTION

The present invention relates to cloned T-type calcium channels.

BACKGROUND OF THE INVENTION

15 Biological membranes are themselves generally impermeable to ionic species. Thus, ions enter cells through regulated pores formed from membrane-associated proteins. Most of these regulated pores are voltage-dependent and are thus able to transduce changes in the transmembrane potential into ion flux. Voltage-gated ion channels form a "superfamily" of related proteins (cf. Jan et al., *Nature*, 345, 672 (1990)). Peculiar to this genus is a high degree of conservation in molecular structure. Generally, voltage-gated channels are membrane bound glycosylated proteins formed of many subunits. Large α subunits form a pore in the membrane that is selective for a given ionic species. Each α subunit contains four domains (I, II, III, and IV). Each channel domain has six putative transmembrane helical segments (S_1-S_6). In general, 20 the segments within each domain are similar but not identical. Aside from overall structural conservation, certain charged residues within the domains are highly conserved among voltage-gated ion channels (Jan et al., *supra*; Stühmer et al., *Nature*, 339, 597-603 (1989)).

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Differences in charged residues between groups of voltage-gated ion channels 30 confer properties unique to each subgroup, such as ion selectivity. For example, most voltage gated ion channels are selective for either sodium, potassium or calcium. Known calcium channels require a ring of negative charge provided by glutamate residues found at similar locations in each of the domains (Yang et al., *Nature*, 366, 158-61 (1993)).

35 Voltage-gated channels are often classified on the basis of their electrophysiology. The resting membrane potential of most animal cells is between about -70 mV and -80 mV. When the membrane becomes depolarized (moved towards 0 mV), various membrane channels become activated (they are said to

“open”). Thus, one basis for classifying membrane channels is the membrane potential necessary to activate (or “gate”) them (voltage dependency). For example, “T-type” calcium channels are activated at a lower voltage than L- or N-type channels (Nowycky et al., *Nature*, 316, 440-43 (1985)). Other physiological properties are the activation kinetics, inactivation kinetics, tail current (deactivation kinetics), and single channel conductance. Thus, in comparison to other calcium currents, T-type calcium current is characteristically short (Chen et al., *J. Gen. Physiol.*, 96, 603-30 (1990)), and it exhibits characteristically slow activation kinetics near threshold, fast inactivation kinetics, and slow tail current (Randall et al., *Neuropharmacol.*, 63, 10 879-93 (1997); Carbone et al., *Nature*, 310, 501-02 (1984); Nilius et al., *Nature*, 316, 443-46 (1985)).

Calcium currents have been implicated in many neurological and muscular functions. For example, T-type calcium current is associated with cardiac pacemaker activity, pain transmission in the central nervous system, and in other physiological functions. Defects in T-type calcium current have been implicated in cardiac arrhythmia, hypertension, and epilepsy. Given their potential clinical value, the pharmacological properties of calcium channels have been the subject of extensive study. Most such studies have involved L-type channels because, unlike T-type channels, L-type calcium channels are readily purified from cell extracts. For example, L-type calcium channels have been purified using dihydropyridine drugs (e.g., nifedipine) which can bind with sufficiently high affinity to serve as a ligand for purifying L-type calcium channels. Such purified and cloned L-type calcium channels have been used to develop assays for drugs affecting L-type calcium channels (see, e.g., U.S. Patents 5,429,921 and 5,386,025).

While many electrophysiological characteristics of T-type calcium currents are known, the lack of isolated T-type channels has stalled research into the pharmacology and biophysics underlying the T-type calcium current, at least in comparison with other calcium channels. Indeed, while it is generally assumed that voltage-sensitive ion channels are responsible for the current, no such channel protein, nor any nucleic acid encoding such a protein, has been isolated. In view of the foregoing problems, there exists a need for an isolated T-type calcium channel and a nucleic acid encoding a T-type calcium channel.

BRIEF SUMMARY OF THE INVENTION

The present invention provides an isolated or substantially purified nucleic acid encoding a protein comprising at least one domain of a T-type calcium channel and cells and cell lines expressing such nucleic acids. The present invention also provides an isolated or substantially purified T-type calcium channel and an isolated or

substantially purified antibody molecule recognizing an epitope on a T-type calcium channel protein.

The present invention is useful for exploring the electrophysiology and pharmacology of the T-type calcium current. Such knowledge can lead to the development of drugs for potentiating or attenuating T-type calcium channels. Thus, the present invention provides an assay for identifying potential drugs affecting T-type calcium channels by exposing cells expressing a T-type calcium channel to a putative drug and then measuring the calcium flux in response to a change in membrane potential. The identification of drugs affecting T-type calcium channels will facilitate even greater understanding of the biophysics of these proteins. Furthermore, some such drugs could have potential clinical applications.

The invention can best be understood with reference to the accompanying drawings and in the following detailed description of the preferred embodiments.

15 BRIEF DESCRIPTION OF THE DRAWINGS

Figures 1A-1E compare the complete amino acid sequences of three types of T-type calcium channels ($\alpha 1G$ (or $Ca_vT.1$), $\alpha 1H$ (or $Ca_vT.2$), and $\alpha 1I$ (or $Ca_vT.3$)), indicating conserved functional domains.

Figures 2A-2D are graphic representations of the current-voltage relationships of three cloned T-type calcium channels (Figures 2A, 2B, and 2C) and a cloned R-type calcium channel (Figure 2D).

Figure 3A is a graphic representation of the average current-voltage curve for cloned T-type calcium channels ($\alpha 1G$, triangles, $\alpha 1H$, inverted triangles, $\alpha 1I$, circles), and a cloned R-type calcium channel (filled squares). Figure 3B compares the normalized conductance of a cloned T-type calcium channel at three different concentrations of $BaCl_2$.

Figure 4 depicts average kinetics of the tail current as a function of repolarization potential for $\alpha 1G$ (triangles), $\alpha 1H$ (inverted triangles), $\alpha 1I$ (circles), and a cloned R-type calcium channel (filled squares).

Figures 5A and 5B graphically present data concerning the use of a cloned T-type calcium channel to detect drugs affecting the channel. Figure 6A depicts the effect of 100 μM on current-voltage relationships with a single dosage of miberfradil. Figure 6B illustrates the effect on T-type channel conductance of various doses of miberfradil.

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DESCRIPTION OF THE PREFERRED EMBODIMENTS

The present invention provides an isolated or substantially purified nucleic acid encoding a protein comprising at least one domain of a T-type calcium channel α

subunit. The nucleic acid can be of any type, and it can include other elements aside from a sequence encoding a T-type calcium channel domain or domains. For example, where the nucleic acid comprises RNA, it can also include regulatory sequences suitable to permit translation of the RNA. Thus, an RNA nucleic acid of the present invention preferably has at least one ribosome entry site, and preferably has a polyadenosine tail for stabilizing the RNA in the cellular environment.

5 Similarly, DNA nucleic acids of the present invention can have regulatory elements for promoting the transcription of sequence encoding the T-type calcium channel into an RNA such as that described above. For example, a DNA nucleic acid of the present invention can have a promoter and/or an enhancer sequence. While the nucleic acid can be any type of nucleic acid, the nucleic acid preferably comprises a cDNA. A cDNA nucleic acid is preferred over other nucleic acids to permit the nucleic acid to be readily cloned, sequenced, and expressed in a wide variety of cells.

10 The choice of promoter and/or an enhancer will largely depend on the milieu in which the nucleic acid is to be expressed. Thus, for expression in bacterial cells, the regulatory elements are bacterial promoters. Similarly, for expression in mammalian cells, the regulatory elements are able to effect expression in mammalian cells. While many such regulatory elements are known in the art, examples include prokaryotic promoters and viral promoters (e.g., retroviral ITRs, LTRs, immediate early viral promoters (IEp), such as herpesvirus IEp (e.g., ICP4-IEp and ICP0-IEp), cytomegalovirus (CMV) IEp, and other viral promoters, such as Rous Sarcoma Virus (RSV) promoters, and Murine Leukemia Virus (MLV) promoters). Other suitable promoters are eukaryotic promoters, such as enhancers (e.g., the rabbit β -globin regulatory elements), constitutively active promoters (e.g., the β -actin promoter, etc.), signal specific promoters (e.g., inducible promoters such as a promoter responsive to RU486, etc.), and tissue-specific promoters (e.g., those active in epidermal tissue, dermal tissue, tissue of the digestive organs (e.g., cells of the esophagus, stomach, intestines, colon, etc., or their related glands), smooth muscles, such as vascular smooth muscles, cardiac muscles, skeletal muscles, lung tissue, hepatocytes, lymphocytes, endothelial cells, sclerocytes, kidney cells, glandular cells (e.g., those in the thymus, ovaries, testicles, pancreas, adrenals, pituitary, etc.), tumor cells, cells in connective tissue, cells in the central nervous system (e.g., neurons, neuralgia, etc.), cells in the peripheral nervous system, and other cells of interest).

15 The isolated or substantially purified nucleic acid of the present invention encodes all or part of a T-type calcium channel α subunit. As used herein, a "calcium channel" includes a protein structure for facilitating the flux of calcium ions across a biological membrane into which the calcium channel is inserted. As used herein, a "T-type channel" is a type of voltage-gated ion channel that facilitates the flux of ions

when the membrane potential of a biological membrane into which it is inserted experiences a slight depolarization. Thus, a T-type calcium channel can begin to gate from about -60 mV to about -30 mV (i.e., about -45 mV to about -35 mV) in about 10 mM Ba²⁺. Additionally, T-type channels of the present invention exhibit a slow deactivation (tail current) following depolarization. Thus, a T-type calcium channel can exhibit a tail current that decays exponentially with a tau value from about 1 ms to about 10 ms (e.g., from about 4 ms to about 7 ms, such as about 6 ms) following repolarization to a membrane potential from about -80 mV to about -60 mV in a solution with a Ba²⁺ concentration of from about 10 mM to about 40 mM. Another defining characteristic of T-type calcium channels is that they exhibit small single channel conductance. Thus, for example, a T-type channel exhibits a single channel conductance of from about 4 pS to about 12 pS (e.g., from about 6 pS to about 10 pS), and typically from about 7 pS to about 9 pS in a solution with a Ba²⁺ concentration of about 0.1 M.

The isolated or substantially purified nucleic acid of the present invention encodes all or part of any T-type calcium channel having at least one of the aforementioned electrophysiological properties when properly assembled within a cellular membrane. The general structure of calcium channels is summarized above and is otherwise known in the art. Thus, for example, the nucleic acid can encode one of the four functional domains mentioned above. As used herein, a domain of a T-type calcium channel is any protein structure able to associate with three other domains to form a tetrameric body functioning as a T-type calcium channel. While the native T-type calcium channel structure includes all four domains in a single polypeptide (indicated in Figures 1A-1E), a domain can exist as a polypeptide species separate from those containing the other domains. Such separate domains are able to associate within the plasma membrane to form a functional channel. Alternatively, where a plurality of domains are linked within a common polypeptide, the linkage can deviate substantially from the native linkage. Thus, for example, the domains can be linked by polypeptide sequences other than those sequences linking the domains in the native protein (e.g., non-native polyglutamate linkages). Indeed, the domains themselves can include non-native linkages between membrane-spanning elements within the domains. Aside from these modifications, the nucleic acid can encode a chimeric calcium channel domain (or an entire channel) comprising a portion of a T-type calcium channel and a portion derived from another calcium channel (or other channel) protein. For example, the chimera can include portions of domains from T-type channels responsible for low voltage gating and portions of domains from other calcium channels responsible for slow inactivation. Such a protein exhibiting T-type gating but longer inactivation kinetics would facilitate pharmacological research.

As mentioned, nucleic acids of the present invention can encode an entire T-type channel (i.e., a T-type channel protein comprising four functional domains). It has been discovered that at least three genes encoding T-type calcium channels exist in humans and rats (i.e., $\alpha 1G$ (or $Ca_vT.1$): $\alpha 1H$ (or $Ca_vT.2$), and $\alpha 1I$ (or $Ca_vT.3$)), and alternate splicing of these isoforms exist. Examples of the amino acid sequences of full-length T-type channels, and the sequences of suitable coding nucleic acids are set forth at SEQ ID NOS:1-8 ($\alpha 1G$ sequences), SEQ IS NOS:9-10 ($\alpha 1H$ sequences), and SEQ ID NOS: 11-12 ($\alpha 1I$ sequences). However, the invention is not limited to these exemplary sequences. Indeed, as mentioned, an amino acid sequence of a T-type calcium channel can vary from those listed, and it is within the state of the art to change a nucleotide sequence encoding a T-type channel to introduce mutations into the protein. Indeed, for conducting electrophysiological assays, it may be desirable to introduce mutations into such a protein. For example, mutations comprising insertions or deletions can be introduced on either the amino- or carboxy-terminus of the protein, or such mutations can be intrasequence insertions or deletions. Where the electrophysiological properties of the calcium channel are to be conserved, such mutations preferably are in regions other than the membrane spanning domains. However, in some applications (e.g., to decrease inactivation kinetics), the changes can be within the membrane-spanning regions. Moreover, as mentioned above, the sequence can form a protein having only one functional domain of a T-type calcium channel. Additionally, the sequence can also form a chimeric protein or domain, such as those described above.

Aside from insertions and deletion mutations of native T-type calcium channel sequences, a T-type calcium channel can include substitutions of amino acid residues, e.g., for those indicated in SEQ ID NOS:1-12. Preferably, and especially where such a substitution is within a membrane spanning region, the substitution is conservative. Thus, within membrane spanning domains, positively-charged residues (H, K, and R) preferably are only substituted with positively-charged residues; negatively-charged residues (D and E) preferably are only substituted with negatively-charged residues; neutral polar residues (C, G, N, Q, S, T, and Y) preferably are only substituted with neutral polar residues; and neutral non-polar residues (A, F, I, L, M, P, V, and W) preferably are only substituted with neutral non-polar residues. Preferably, any amino-acid substitution within the membrane-spanning regions does not alter this conservation. Most preferably, any substitution, deletion, or insertion does not alter the IVS4 domain. In each of the exemplary T-type calcium channel α subunit sequences, the putative IVS4 region comprises SEQ ID NO:13. Given the strong sequence conservation among families of voltage-gated ion channels, it is likely that this sequence or a derivative sequence, will be present in T-type channels. Thus, the

present invention provides any T-type calcium channel (or a nucleic acid encoding such a T-type calcium channel) comprising SEQ ID NO:13 or a sequence derived from SEQ ID NO:13 having conservative amino acid substitutions, as described above.

5 The nucleic acid of the present invention encoding all or a part of a T-type calcium channel can be isolated via any suitable method. For example, prior to the present invention, one of skill in the art could design a probe based on the sequence of known, non-T-type, calcium channels and use such probe to screen a genetic library. If such a screen were to identify a putative calcium channel, the researcher could then
10 attempt to clone the entire nucleic acid to characterize it. Similarly, prior to the present invention, to isolate a nucleic acid encoding a T-type calcium channel, one of skill in the art could consult publicly available databases containing DNA sequences (e.g., Genbank) to locate nucleic or amino acid sequences representing a portion of a T-type calcium channel protein or nucleic acid. However, such databases contain no
15 sequence for a full-length T-type calcium channel or identify any sequence as a T-type channel. Such methods assume that T-type calcium channels share sufficient sequence identity with known calcium channel nucleic acids to cross-hybridize, an assumption not supported by any published report. Moreover, prior to the present invention, no partial sequence in such databases was identified as corresponding to a
20 T-type calcium channel. Thus, prior to the present invention, the presence of partial sequences in the public DNA databases could facilitate the isolation of T-type calcium channels only with the exercise of a considerable degree of speculation on the part of the researcher.

25 By providing several sequences pertaining to T-type calcium channels and a comparison presenting conserved regions and domains, the present invention greatly facilitates the isolation of other nucleic acids encoding T-type calcium channels (or derivatives thereof) with much less experimentation. Thus, while any of the methods discussed above can be employed to isolate other members of this genus, preferably, a nucleic acid encoding a T-type calcium channel is isolated by probing a genetic library
30 using a probe that hybridizes to a DNA encoding a peptide sequence contained in (or similar to) a known T-type calcium channel (e.g., SEQ ID NOS:1-12). To facilitate the isolation of a T-type calcium channel, the present invention provides an isolated polynucleotide hybridizing to a portion of the nucleic acid of the present invention encoding a T-type calcium channel (or a portion thereof). Thus, for example, the
35 present invention includes an isolated polynucleotide hybridizing to SEQ ID NO:1-12. The isolated polynucleotide can hybridize to all or any portion of the sequence encoding the T-type calcium channel.

To isolate such a polynucleotide, any portion of a sequence encoding a T-type calcium channel can be employed as a probe to screen a genetic library, and such screening can be accomplished by standard techniques known in the art. While the probe can hybridize to any portion of such a DNA, preferably the probe is designed to 5 hybridize to a DNA encoding a polypeptide sequence that is highly conserved among T-type calcium channels but is less conserved between the genus of T-type calcium channels and other proteins. Such peptide sequences are readily apparent from the sequence comparison set forth in Figures 1A-1E. Generally, the specificity of hybridization in a genetic screen varies depending on the length of the probe and the 10 stringency (e.g., temperature, salt and detergent concentration, etc.) of hybridization. Stringency of hybridization is broadly classified as "high," "moderate," or "low," and the parameters of these terms are well recognized in the art (see, e.g., Sambrook et al., "Molecular Cloning, a Laboratory Manual," Cold Spring Harbor Press, 1989). The 15 isolated polynucleotide hybridizing to a portion of the nucleic acid encoding a T-type calcium channel can hybridize under any desired stringency conditions. However, for identifying other T-type channels, preferably, the hybridization occurs under moderate stringency, and most preferably under high stringency.

Of course, the isolated or substantially purified polynucleotide can itself be employed as a probe to screen a library as described to isolate a second nucleic acid. 20 In such a screen, one of the polynucleotides will be complementary to a portion of the sequence encoding the T-type calcium channel, and the other isolated nucleic acid will be "sense." Preferably, one of the two isolated polynucleotides (the "sense" strand) itself encodes a T-type calcium channel, or at least one domain thereof. Such a sequence can be cloned to be operably linked to suitable regulatory elements, as 25 described, to produce a T-type calcium channel. Thus, aside from using the nucleic acid of the present invention to produce a T-type calcium channel, the nucleic acids of the present invention are also useful for isolating other sequences encoding T-type calcium channels, or derivatives thereof.

However isolated, the isolated or substantially purified nucleic acid of the 30 present invention is useful, in part, for producing all or a portion of a T-type calcium channel. Thus, the nucleic acid can be introduced into a suitable milieu for driving its expression. Because T-type channels are transmembrane proteins, preferably such a milieu is a living cell. However, it should be understood that the nucleic acid can also be expressed *in vitro* under conditions, such as those known in the art, suitable for *in* 35 *vitro* transcription and translation. However produced, the present invention includes any protein, such as a recombinant protein or an isolated or substantially purified protein, including all or a portion of a T-type calcium channel or a protein derived from a T-type calcium channel.

For expression in a living cell, the nucleic acid must be introduced into the cell. As nucleic acids are generally introduced into cells as part of genetic vectors, the present invention provides a vector having a T-type calcium channel nucleic acid of the type described above. Any type of vector suitable for introducing the nucleic acid into a host cell is within the context of the present invention. Examples of such vectors include naked DNA and RNA vectors (such as oligonucleotides, plasmids, capped cRNA, etc.), viral vectors such as adeno-associated viral vectors (Berns et al., *Annals of the New York Academy of Sciences*, 772, 95-104 (1995)), adenoviral vectors (Bain et al., *Gene Therapy*, 1, S68 (1994)), herpesvirus vectors (Fink et al., *Ann. Rev. Neurosci.*, 19, 265-87 (1996)), packaged amplicons (Federoff et al., *Proc. Nat. Acad. Sci. USA*, 89, 1636-40 (1992)), papilloma virus vectors, picornavirus vectors, polyoma virus vectors, retroviral vectors, SV40 viral vectors, vaccinia virus vectors, and other vectors. Once a given type of vector is selected, its genome must be manipulated for use as a background vector, after which it must be engineered to incorporate exogenous polynucleotides. Such manipulations are known in the art.

The vectors of the present invention are useful for introducing a nucleic acid encoding all or a portion of a T-type calcium channel into a host cell. Thus, the present invention provides a cell into which the vector of the present invention has been introduced. The host cell can be any cell suitable for expressing the nucleic acid (e.g., bacteria, insect cells, mammalian cells, etc.). The host cell can thus be *in vitro* or *in vivo*. Preferably the cells do not exhibit native T-type calcium current. A preferred cell type is HEK-293 cells because they contain genetic elements that facilitate the expression of transgenes from a variety of expression vectors. For facilitating electrophysiological recordings, oocytes (e.g., *Xenopus* oocytes) are preferred, as they are large and readily handled.

The vector can be introduced into the cell in any manner suitable for the cell type and vector employed. In one embodiment, the vector can be used to prepare an RNA transcript *in vitro* (e.g., a capped cRNA) which is then introduced into the host cell by standard methods (such as injection). Such techniques are preferred when the host cells do not actively transcribe DNA (such as oocytes). In other embodiments, a DNA vector is introduced into the cell such that it is transcribed within the cell. For example, the vector can be introduced into the cell such that it forms an extrachromosomal segment of genetic material in the cell, as is the case with many types of viral vectors. Alternatively, the vector can introduce the nucleic acid into the chromosomal DNA of the host cell.

Preferably, a cell into which the nucleic acid is introduced is also able to express the nucleic acid to produce the α subunit protein. The expression of the nucleic acid can be detected by probing the cell for the presence of T-type calcium

channel mRNA, such as via Northern hybridization analysis, in situ hybridization, etc. More preferably, however, the cell is able to express the nucleic acid to produce the protein including all or a portion of a T-type calcium channel. In such cells, expression of the nucleic acid is confirmed by detecting the protein, for example, by probing cellular extracts with an antibody recognizing the protein (e.g., on a Western blot, etc.).

In the membrane of the cell producing the protein, the expressed protein contributes to the formation of a functional calcium channel. Where the protein encodes an entire α subunit, the full protein will possess some or all of the electrophysiological properties of T-type calcium channels described above. Where the protein encodes less than an entire channel α subunit (e.g., a domain), the protein will aggregate with other constituent domains in the membrane to form a functional channel. Thus, the presence of the protein can be detected by assaying the cell for T-type calcium channel activity. Indeed, assaying for channel activity serves to determine whether a nucleic acid encoding a putative calcium channel, in fact, encodes a species of T-type channel (as opposed to a member of another genus of calcium channels). For example, when large cells (e.g., oocytes) are used as the host cells, the electrophysiological properties of the channel can be investigated. Thus, the membrane activity of whole cells expressing the nucleic acid can be measured directly, such as via patch clamp techniques using a voltage clamp electrode and a current electrode (Bernal et al., *J. Pharmacol. Exp. Ther.*, 282, 172-80 (1997)). Alternatively, the activity of single channels can be measured, such as with a standard depolarizing bath and pipette solutions (Lacerda et al., *Biophys. J.*, 66, 183-43 (1994)). However measured, the properties of cells into which the putative nucleic acid is introduced are compared to the channel conductance, voltage dependency, activation kinetics, inactivation kinetics, or tail current known for T-type channels and discussed above. A measure of current density (e.g., pA/pF) can also be used to assess the level of gene expression in the cells, normalizing for cellular volume.

While, in accordance with the present invention, an isolated cell into which the T-type calcium channel nucleic acid has been introduced (and preferably stably expressing the nucleic acid to produce the protein) can be prepared, preferably, such transfection protocols result in a population consisting essentially of such transfected cells. For standardizing the results of many experiments, it is even more desirable to employ an established cell line consisting essentially of such cells. Preferably, for use in high throughput assays, cell lines stably expressing a T-type calcium channel exhibit a current density of at least about 40 pA/pF (e.g., at least about 45 pA/pF), such as about 50 pA/pF or even 55 pA/pF or higher. Preferably, a cell line in accordance with the present invention is able to propagate the nucleic acid through

several passages (e.g., for at least 10 passages), and, preferably, the nucleic acid is stably integrated into the chromosomes of such cells. Thus, the cell line can propagate the nucleic acid for at least 20 passages, and more preferably significantly more than 20 passages (e.g., at least about 25 passages, or even more).

5 Regardless of the cell system, the ability to express a T-type calcium channel nucleic acid within host cells to produce an active channel permits the channel to be further studied. In this regard, the present invention provides a method of identifying a drug which affects T-type calcium channels. The method involves first expressing a T-type calcium channel in a cell to produce an active channel, as herein described.

10 The cell expressing the channel is then exposed to a solution containing a putative drug for interfering with the channel. Thereafter, the presence or absence of calcium flux in response to a change in membrane potential is assayed. Any such assay can be employed within the context of the present invention, (e.g., using labile dyes, radioisotopes (e.g., ^{45}Ca), recording electrophysiological changes in the membrane,

15 etc.). A quick method of assaying for calcium flux is first to introduce a calcium-sensitive labile dye into the cells. For example, the dye can be one such as those that fluoresce or change color in the presence of calcium, many of which are known to those of skill in the art (e.g., Indo-1). Thereafter, the cells are exposed to a depolarizing solution containing high (e.g., about 50 mM) potassium concentration

20 and a drug, and the reaction of the labile dye is compared to control cells. Using a labile dye affords the ability to assay many putative drugs quickly in a high throughput assay for putative drugs affecting T-type channels. For example, the initial screening can be carried out in 96 well plates. Moreover, dose-response data can be readily generated by exposing the cells to several concentrations of the same putative

25 drug.

Once a putative drug is detected, its effect on the electrophysiology of the cell (e.g., single channel conductance, voltage dependency, activation kinetics, inactivation kinetics, and tail current of the cells) can be investigated in detail.

Generally, the effect of the putative drug on T-type calcium currents is assessed by measuring the various electrophysiological parameters in the presence of various concentrations of the drugs and comparing the data to untreated (or sham-treated) control cells. Cells preferably are maintained in a continuous perfusion chamber during such experiments to facilitate changing solutions. The inventive method of identifying a drug which affects T-type calcium channels can employ any nucleic acid encoding a T-type calcium channel (or derivative thereof), such as those nucleic acids described herein. In fact, as several isoforms of T-type channel exist, the assay method can be repeated using nucleic acids encoding different isoforms to identify

drugs that preferentially target a given isoform, or drugs which affect more than one isoform of T-type calcium channels.

Aside from affording an *in vitro* assay for detecting potential therapeutic or investigative drugs targeting T-type calcium channels, the method of expressing the T-type calcium channel nucleic acid can also be used *in vivo*. For example, as mentioned, several neurological and muscular diseases or disorders have implicated mutations affecting native nucleic acids encoding T-type calcium channels. The present invention, thus, provides a method of treating a disease or disorder associated with a deficiency in a native T-type calcium channel nucleic acid. The method involves introducing a vector having the T-type calcium channel nucleic acid into cells of a host in which native expression of the nucleic acid is deficient. Thus, for example, for treating cardiomyopathy associated with deficiencies in T-type calcium channels, the vector is introduced into myocardial cells. Similarly, for treating forms of epilepsy associated with deficiencies in T-type calcium channels, the vector is introduced into neurons (e.g., thalamic neurons). Within the target cells, the nucleic acid within the vector is expressed to produce active T-type calcium channel. By similar methods, an nucleic acid having a sequence antisense to a sequence encoding a T-type calcium channel (or a portion thereof) can be expressed within a cell. The presence of an antisense sequence can down-regulate the expression of native T-type calcium channel genes by hybridizing to T-type channel mRNA within the cell. Thus, the present invention is useful to treating disorders associated with over-expression of T-type calcium channels.

T-type channel proteins (such as whole T-type calcium channels, domains of such channels, chimeras including portions of T-type calcium channels, etc.) can be employed to generate antibodies (e.g., immunoglobulins) to T-type calcium channels. Thus, the present invention provides an isolated and substantially purified antibody molecule recognizing an epitope on a T-type calcium channel. Such antibodies can be monoclonal antibodies or polyclonal antisera. Antibodies recognizing T-type calcium channels can be used to purify the channels from cell extracts or other solutions by standard methodologies (e.g., immunoprecipitation). Moreover, depending on the location of the epitopes for the antibodies on the T-type calcium channel, the antibodies can be used to affect the channel proteins present on the surface of cells. Thus, antibodies directed to T-type calcium channels are potential reagents for studying the channels as well as for therapy.

Such antibodies can be produced by any suitable method, many of which are well known in the art. Thus, for example, the antibodies can comprise polyclonal antisera obtained from innoculated animals. Alternatively, the antibody molecules can be monoclonal antibodies obtained from a cell line (e.g., a hybridoma cell line). Thus,

the present invention provides a cell which produces such antibodies. Such a cell can be *in vitro* or *in vivo*; however, where the cell is *in vitro*, preferably it is within an established cell line consisting essentially of such cells.

Several examples are presented below to illustrate the invention. Taken together, the examples demonstrate the cloning of twelve novel proteins and their characterization as T-type calcium channel α subunits. These examples are included here for purely illustrative purposes; as such, they are not to be construed so as to limit the scope of any aspect of the invention.

Many procedures employed in the following examples are techniques routinely performed by one of ordinary skill in the art (see generally Sambrook et al., *Molecular Cloning. A Laboratory Manual*, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY (1989)) and are not discussed in detail. However, some reagents and methods deserve specific description. Thus, for example, *in vitro* translation and expression were conducted as described previously (Schneider et al., *Receptors and Channels*, 2, 15 255-70 (1995)). *Xenopus laevis* oocytes were prepared as described previously (Bernal et al., *J. Pharmacol. Exp. Ther.*, 282, 172-80 (1997)). To express proteins, 10 or 30 ng of capped cRNA was injected into the oocytes in a volume of 50 nl. For single channel recording, oocytes were injected with 100 ng capped cRNA and incubated for one week prior to assay.

Cells were voltage clamped using a two-microelectrode voltage clamp amplifier as described (Bernal et al., *J. Pharmacol. Exp. Ther.*, 282, 172-80 (1997)). The standard bath solution contained the following: 40 mM Ba(OH)₂, 50 mM NaOH, 1 mM KOH, 0.1 mM EDTA, and 5 mM HEPES, adjusted to pH 7.4 with methanesulfonate. The osmolality of the 2 mM Ba²⁺ and 10 mM Ba²⁺ solutions was balanced by increasing the NaOH concentration as described (Lory et al., *J. Physiol. (London)*, 429, 95-112 (1990)). Voltage and current electrodes (1.5-1.8 M tip resistance) were filled with 3 M KCl. Except as noted, data were acquired at 4 kHz using the pCLAMP system, and filtered at 1 kHz. Data were analyzed using pCLAMP software. Boltzman fits and linear regression were calculated using Prism.

EXAMPLE 1

This example demonstrates the cloning and characterization of putative T-type calcium channels.

A search of the Genbank library was conducted to identify clones identified as having some degree of homology to known calcium channel sequences. The search identified an expressed sequence tagged (EST) partial sequence in a human brain clone (H06096), which was used as a probe to screen a λ gt10 cDNA library prepared

from rat brain. Successive screening of the cDNA library identified five overlapping clones which were aligned to construct an entire cDNA sequence, termed α 1G.

The α 1G cDNA was cloned into the pSP72TM vector and sequenced by standard computer-assisted sequencing. Using the α 1G cDNA, the amino acid sequence of the α 1G protein was deduced and compared to the sequences of other known calcium channel α subunits. By similar methods, homologous human (H19230 and R19524) and mouse (AA286626) EST clones were also identified and partially sequenced, and alternately spliced variants were identified. The deduced cDNA and amino acid sequences for eight full-length α 1G T-type channels are set forth, respectively, as SEQ ID NOS:1-8.

A second T-type calcium channel, termed α 1H, was isolated by screening a human heart cDNA library with a fragment of the α 1G sequence. An alternately spliced isoform was also identified. The full-length cDNA and amino acid sequences for these α 1H T-type channels are set forth, respectively, as SEQ ID NOS:9 and 10.

A third T-type calcium channel, termed α 1I, was isolated by screening a rat brain cDNA library at low stringency using a fragment of the rat α 1G gene. Fifty plaques were identified, many of which were not detected in a second screening. A third screening with a fragment from α 1H identified two clones. Subsequent screening, and the use of the GenBank database, led to the identification of the full length rat and human cDNA and amino acid sequences, set forth at SEQ ID NOS: 11 and 12, respectively.

The α 1G, α 1H, and α 1I amino acid sequences were compared to each other and a known calcium channel (α 1E) to investigate the conservation of protein structure and function. The comparison indicates that the α 1G, α 1H, and α 1I amino acid sequences within the putative membrane-spanning domains are about 90 % identical to each other, while the α 1G, α 1H, and α 1I sequences are only roughly 40 % identical to the α 1E clone.

Figures 1A-1E indicate this conservation between the proteins. The conservation of charged residues, particularly in the S4 domains, is consistent with the role of the α 1G, α 1H, and α 1I proteins as ion channels. However, two of the glutamates associated with ion specificity in other calcium channels have been replaced with aspartate, suggesting altered ion selectivity. Strikingly, α 1G, α 1H, and α 1I display only low homology to sequences linking the membrane-spanning regions within each domain, and even less homology between the intracellular loops linking domains. Notably, neither α 1G, α 1H, nor α 1I possesses sequences known to bind β subunits or Ca^{2+} ions.

EXAMPLE 2

This example demonstrates the production of cell lines stably expressing the cloned $\alpha 1G$, $\alpha 1H$, and $\alpha 1I$ proteins.

HEK-293 cells were transfected with either the rat $\alpha 1G$ cDNA (SEQ ID

- 5 NO:1), the human $\alpha 1H$ cDNA (SEQ ID NO:9), or the rat $\alpha 1I$ cDNA (SEQ ID NO:11). As a control, cells were also transfected with human $\alpha 1E$ plus human $\beta 3$ (Schneider et al., *Receptors Channels*, 2, 255-70 (1994); Murakami et al., *Eur. J. Biochem.*, 236, 138-43 (1996)). The DNA constructs included a neomycin resistance gene conferring resistance to G418. The cells were cultured under standard conditions
10 using medium containing G418 to select for stable transformants.

Surviving clones were expanded and assayed for electrophysiological activity to determine the presence of channels within the membrane. Whole-cell currents were recorded from ruptured patches using an Axopatch 200A amplifier, Digidata 1200 A/D converter, and pCLAMP 6.0 software. Data were digitized at 2 kHz and filtered
15 at 1 kHz or off-line. All experiments were performed at room temperature. Pipettes were made out of TW-150-6 capillary tubing (World Precision Instruments, Inc., Sarasota, FL), using a Model P-97 Flaming-Brown pipette puller (Sutter Instrument Co., Novato, CA). The internal pipette solution contained the following: 55 mM CsCl, 75 mM CsSO₄, 10 mM MgCl₂, 0.1 mM EGTA, 10 mM HEPES, pH adjusted to
20 7.2 with CsOH. The external Tyrodes solution was the following: 140 mM NaCl, 6 mM KCl, 2 mM CaCl₂, 10 mM glucose, 5 mM HEPES, pH 7.4. The recording solution contained the following: 10 mM BaCl₂ solution (or 2 mM CaCl₂), 140 mM tetraethylammonium (TEA) chloride, 5 mM CsCl, 1 mM MgCl₂, 5 mM glucose, and
25 10 mM HEPES, pH adjusted to 7.4 with TEA-OH. Under these solution conditions the pipette resistance was typically 1.5-2.5 M Ω . Cell capacitance was measured by integrating the charging current during a 10 mV hyperpolarizing pulse (holding potential -80 mV).

Using these recording techniques, values for pA/pF were obtained for each cell line, which is a measure of current density normalizing for cell size. One clone (#N2)
30 expressed the rat $\alpha 1G$ protein and has a current density of 42 pA/pF. Another clone (#13), expressed the human $\alpha 1H$ protein and exhibited a current density of 53 pA/pF. Three clones (#11, #19, and #25) expressed the rat $\alpha 1I$ protein and exhibited current densities of 40 pA/pF, 45 pA/pF, and 55 pA/pF, respectively

35 EXAMPLE 3

This example demonstrates that the cloned putative T-type calcium channels exhibit T-type current-voltage relationships.

Current traces were elicited by depolarizing voltage clamp pulses of the membranes of cells. The $\alpha 1G$, $\alpha 1H$, and $\alpha 1I$ proteins were produced in *Xenopus laevis* oocytes by linearizing the DNA vectors containing the coding sequences, and transcribing the coding sequences *in vitro* by standard methods. Oocytes were then injected with the capped RNA.

Figures 2A-2E depict data obtained from these experiments using cells injected with $\alpha 1G$ (Figure 2A), $\alpha 1H$ (Figure 2B), and $\alpha 1I$ (Figure 2C) and $\alpha 1E$ (Figure 2D). These data indicate that cells expressing $\alpha 1G$, $\alpha 1H$, and $\alpha 1I$ exhibit T-type calcium current, while oocytes expressing $\alpha 1E$ as well as uninjected oocytes (Figure 6A) do not.

Current voltage curves were developed using cells injected with $\alpha 1G$, $\alpha 1H$, $\alpha 1I$, and $\alpha 1E$. Figures 3A depicts such data generated in a 10 mM Ba^{2+} test solution. These data were transformed into conductance and fit with a Boltzman equation to determine the midpoint of activation ($V_{0.5}$). Gating potentials for $\alpha 1G$, $\alpha 1H$, and $\alpha 1I$ (-38 \pm 1 mV n=8, -44 mV \pm 1 mV, n=10, and -31 mV \pm 1 mV, n=6, respectively) were in accordance with the gating potential measured for the HEK-293 cells (-41 \pm 1 mV, n=10), while $\alpha 1E$ required significantly more positive potentials to open (-2.6 mV \pm .4 mV, n=3).

To compare the characteristics with published values (Huguenard, *Ann. Rev. Physiol.*, 58, 329-48 (1996)), the $\alpha 1G$ current was recorded at varying concentrations of Ba^{2+} . As indicated in Figure 3B, in solutions containing 2 mM Ba^{2+} , $V_{0.5}$ was -46.5 mV, and the slope factor (k) was 6.6 (n=7). However, when the Ba^{2+} concentration was 40 mM, $V_{0.5}$ was recorded at -21 mV, presumably due to the results of barium on surface charge screening (see, e.g., Wilson et al., *J. Membrane Biol.*, 72, 117-30 (1983)). Similar values were recorded for $\alpha 1H$ and $\alpha 1I$.

These results indicate that $\alpha 1G$, $\alpha 1H$, and $\alpha 1I$ are low-voltage activated calcium channels (i.e., from about -60 mV to about -30 mV in 10 mM Ba^{2+}).

EXAMPLE 4

This example demonstrates that the cloned putative T-type calcium channels exhibit T-type tail current.

Tail current was measured at -90 mV after first opening the channels with a voltage step to -10 mV. The voltage-dependence of tail current in cells expressing $\alpha 1G$ (oocytes) $\alpha 1H$ (HEK 293 cells), and $\alpha 1I$ (HEK 293 cells) was measured at varying test potentials. As a control, tail current was also measured from a high voltage activated channel $\alpha 1E$, which Raw data from recordings data were fit with a single exponential and plotted as a function of depolarization potential (Figure 4).

These results demonstrate that the tail currents for the cloned $\alpha 1G$, $\alpha 1H$, and $\alpha 1I$ calcium channels are voltage-dependent, consistent with known T-type calcium tail currents. Additionally, these data demonstrate that the tail current for each of the cloned channels is between about 1 ms and about 10 ms following repolarization to a membrane potential from about -80 mV to about -60 mV in a solution with a barium concentration of from about 10 mM to about 40 mM.

EXAMPLE 5

This example demonstrates that the cloned putative T-type calcium channels exhibit T-type single channel conductance.

Measurement of single channel conductance is complicated by the low probability of channel opening at negative potentials when the driving force is large. Thus, single channel conductance was measured similarly for measurements of tail currents to enhance channel opening at negative potentials. Single channels were measured with standard depolarizing bath and pipette (115 mM BaCl₂, 1 mM EGTA, and 10 mM HEPES, pH 7.4) solutions (Lacerda et al., *Biophys. J.*, 66, 1833-43 (1994)). Data were analyzed with TRANSIT (VanDongan, *Biophys J.*, 70, 1303-15 (1996)). Single channel amplitudes were measured by averaging the values obtained from Gaussian fits to all-points histograms of traces with openings, selected openings, or amplitude histograms of idealized openings. It has been reported that some oocytes contain a native 9 pS channel. These endogenous channels can be distinguished by their 2-fold larger current amplitudes at the potentials tested (e.g., -20 mV, $i = 0.8$ for endogenous channels as opposed to 0.4 pA for $\alpha 1G$). However, such endogenous channels were not detected either at the whole cell or single channel level in the oocytes tested.

Current through the main open state of each open channel was measured at each potential and plotted against each test potential. Single channel currents for several patches were then averaged and plotted as a function of test potential, wherein the slope of the plot indicated the single channel conductance. The average slope conductance of the $\alpha 1G$ channel was measured at 7.5 ± 1.5 pS, which corresponds with the reported values for T-type calcium channels (Huguenard, *Ann. Rev. Physiol.*, 58, 329-48 (1996)). Similar results were also obtained with both $\alpha 1H$ (10.8 ± 1.4 pS). Data collected from recordings of the $\alpha 1I$ channels indicate that they open to two distinct amplitudes. The conductance for the small amplitude $\alpha 1I$ openings was measured at 3.9 ± 0.5 pS, while that for the large $\alpha 1I$ openings was measured at 11.4 ± 0.5 pS).

These results indicate that the cloned $\alpha 1G$, $\alpha 1H$, and $\alpha 1I$ proteins exhibit T-type single-channel conductance (e.g., from about 4 to about 12 pS).

EXAMPLE 6

This example demonstrates that a cloned T-type calcium channel can be used for identifying a drug which affects T-type calcium channels.

5 HEK-293 cells were subjected to treatment as indicated above in Example 3, except that an experimental group of cells were exposed to a solution containing 1 μ M mibepradil, a known inhibitor of T-type calcium current. As depicted in Figure 5A, the presence of mibepradil almost completely abolished T-type current in cells expressing $\alpha 1G$. Cells expressing either $\alpha 1G$ or $\alpha 1H$ were similarly treated using
10 various concentrations of mibepradil to determine a dose-response relationship. These results, depicted in Figure 5B, demonstrate that about 50% inhibition was achieved at a mibepradil concentration of 1 μ M.

15 All of the references cited herein, including patents, patent applications, and publications, are hereby incorporated in their entireties by reference.

While this invention has been described with an emphasis upon preferred embodiments, it will be obvious to those of ordinary skill in the art that variations of the preferred embodiments may be used and that it is intended that the invention may be practiced otherwise than as specifically described herein. Accordingly, this
20 invention includes all modifications encompassed within the spirit and scope of the invention as defined by the following claims.

What is claimed is:

1. A isolated or substantially purified nucleic acid encoding a protein comprising at least one domain of a T-type calcium channel α subunit.
- 5 2. The nucleic acid of claim 1, wherein said protein comprises an entire T-type calcium channel α subunit.
3. The nucleic acid of claim 2, wherein said protein comprises SEQ ID NO:13.
- 10 4. The nucleic acid of any of claims 1-3, wherein said calcium channel begins to gate from about -60 mV to about -30 mV in 2 mM Ba²⁺.
5. The nucleic acid of any of claims 1-4, wherein said calcium channel exhibits a tail current of from about 1 ms to about 10 ms following repolarization to a membrane potential from about -80 mV to about -60 mV in a solution with a barium concentration of from about 10 mM to about 40 mM.
- 15 6. The nucleic acid of any of claims 1-5, wherein said calcium channel exhibits a single channel conductance of from about 4 pS to about 11 pS in a solution with a barium ion concentration of about 100 mM.
7. An isolated or substantially purified nucleic acid hybridizing to the nucleic acid of any of claims 1-6.
- 20 8. An isolated or substantially purified nucleic acid hybridizing to the nucleic acid of claim 7.
9. The nucleic acid of claim 8 comprising a sequence encoding at least one domain of a T-type calcium channel α subunit.
10. A vector comprising the nucleic acid of any of claims 1-9.
- 25 11. A cell into which the vector of claim 10 has been introduced.
12. The cell of claim 11, which expresses said nucleic acid to produce said protein.
13. The cell of claim 11 or 12, which stably expresses said nucleic acid to produce said protein.
- 30 14. A population of cells consisting essentially of cells according to any of claims 11-13.
15. An established cell line consisting essentially of cells according to any of claims 11-13.
- 35 16. A method of identifying a drug which affects T-type calcium channels, said method comprising expressing a T-type calcium channel in a cell, exposing said cell to a putative drug, and measuring the calcium flux through the membrane of said cell in response to a change in membrane potential.

17. The method of claim 16, wherein said calcium flux is assayed by using a calcium-sensitive labile dye within said cell.

18. The method of claim 16, wherein said calcium flux is assayed by measuring the electrophysiological properties of said cell.

5 19. The method of claim 16, wherein said calcium channel comprises SEQ ID NO:13.

20. An isolated or substantially purified immunoglobulin recognizing an epitope on a T-type calcium channel protein.

21. A cell *in vitro* which produces the immunoglobulin of claim 20.

10 22. An established cell line consisting essentially of cells according to claim
21.

hCavT1a MDEEDGAGAEE SGOPR-----
 rCavT1a MDEEDGAGAEE SGOPR-----
 hCavT2a MTEGARAADAEVRVPLGRRPMPCCGGVPGE PRRGACTRGCGCGELGVSPSESSPAERCAELGADEEQRVYPALAATVFCLQTTPRSWCLRLVCNPW
 hCavT3 MAESAPPSSAAA-----
 rCavT3 MADSNLPPSSAAAAP-----
 hCavT1a CRSVPTLRGDG-----
 rCavT1a CRSVPTLRGDG-----
 hCavT2a CSHIPGRDVRMPCTLGWEA-YTOPQA GVGAARNACINWNQYNNCRSGDSNPHNGAINFDNTCYAWIIFQVTLERHMLLEORQYLS-
 hCavT3 CHEIPPLKEQGRECCCLSKDVIDFGAGRODLNASGLCVNWNRYNNCRIGTSANPHKGAINFDNIGYAGIVIFQVTLERHMLLEORQYLS-
 rCavT3 CHEIPPLKEQGRECCCLSKDVIDFGAGRODLNASGLCVNWNRYNNCRIGTSANPHKGAINFDNIGYAGIVIFQVTLERHMLLEORQYLS-
 hCavT1a LLIIVGSEFMINCLVVIATQFSETKORESQLMREQRVRFLSNASTLASFEPGSCYELLKYLVYILRKARRLAQVSRAAGVRLLSSPAPLGGQET
 rCavT1a LLIIVGSEFMINCLVVIATQFSETKORESQLMREQRVRFLSNASTLASFEPGSCYELLKYLVYILRKARRLAQVSRAIGVAGLISSPVARSQGP
 hCavT2a CSHIPGRDVRMPCTLGWEA-YTOPQA GVGAARNACINWNQYNNCRSGDSNPHNGAINFDNTCYAWIIFQVTLERHMLLEORQYLS-
 hCavT3 CHEIPPLKEQGRECCCLSKDVIDFGAGRODLNASGLCVNWNRYNNCRIGTSANPHKGAINFDNIGYAGIVIFQVTLERHMLLEORQYLS-
 rCavT3 LLIIVGSEFMINCLVVIATQFSETKORESQLMREQRVRFLSNASTLASFEPGSCYELLKYLVYILRKARRLAQVSRAIGVAGLISSPVARSQGP
 hCavT1a FERISMVILLNCVTLGMFRPCEDIACDSQRCCRILQAFDDIFIFFAFFAVEMVVKMVALGIFGKKCYLGDFTNRLDFIVIAGMLEYSLDLQNVFSAVRTV
 rCavT1a FERVSIMVILLNCVTLGMFRPCEDIACDSQRCCRILQAFDDIFIFFAFFAVEMVVKMVALGIFGKKCYLGDFTNRLDFIVIAGMLEYSLDLQNVFSAVRTV
 hCavT2a FEHVSMVLMVIMLNCVTLGMFRPCDVECGSERCNILEAFDAFIFFAFFAVEMVVKMVALGIFGKKCYLGDFTNRLDFIVIAGMLEYSLDLQNVFSAVRTV
 hCavT3 FECVSMVLMVILLNCVTLGMYQCPDDMDCLSDRCKTQMVFDDFIF1FFAMEMVVKMVALGIFGKKCYLGDFTNRLDFIVIAGMLEYSLDLQNVFSAVRTV
 rCavT3 RVLRLKAINRVPSMRILVNLLIDTLPMGNVLLLCFFVFFIFGIGVQLWAGLRLRNRCFLEENFTIQGDVA-LPPYYQPEEDEMPPFICSLTGDNIMG
 hCavT1a RVLRLKAINRVPSMRILVNLLIDTLPMGNVLLLCFFVFFIFGIGVQLWAGLRLRNRCFLEENFTIQGDVA-LPPYYQPEEDEMPPFICSLTGDNIMG
 rCavT1a RVLRLKAINRVPSMRILVNLLIDTLPMGNVLLLCFFVFFIFGIGVQLWAGLRLRNRCFLEENFTIQGDVA-LPPYYQPEEDEMPPFICSLTGDNIMG
 hCavT2a RVLRLKAINRVPSMRILVNLLIDTLPMGNVLLLCFFVFFIFGIGVQLWAGLRLRNRCFLEENFTIQGDVA-LPPYYQPEEDEMPPFICSLTGDNIMG
 hCavT3 RVLRLKAINRVPSMRILVNLLIDTLPMGNVLLLCFFVFFIFGIGVQLWAGLRLRNRCFLEENFTIQGDVA-LPPYYQPEEDEMPPFICSLTGDNIMG
 rCavT3 RVLRLKAINRVPSMRILVNLLIDTLPMGNVLLLCFFVFFIFGIGVQLWAGLRLRNRCFLEENFTIQGDVA-LPPYYQPEEDEMPPFICSLTGDNIMG
 hCavT1a FERISMVILLNCVTLGMFRPCEDIACDSQRCCRILQAFDDIFIFFAFFAVEMVVKMVALGIFGKKCYLGDFTNRLDFIVIAGMLEYSLDLQNVFSAVRTV
 rCavT1a FERVSIMVILLNCVTLGMFRPCEDIACDSQRCCRILQAFDDIFIFFAFFAVEMVVKMVALGIFGKKCYLGDFTNRLDFIVIAGMLEYSLDLQNVFSAVRTV
 hCavT2a FEHVSMVLMVIMLNCVTLGMFRPCDVECGSERCNILEAFDAFIFFAFFAVEMVVKMVALGIFGKKCYLGDFTNRLDFIVIAGMLEYSLDLQNVFSAVRTV
 hCavT3 FECVSMVLMVILLNCVTLGMYQCPDDMDCLSDRCKTQMVFDDFIF1FFAMEMVVKMVALGIFGKKCYLGDFTNRLDFIVIAGMLEYSLDLQNVFSAVRTV
 rCavT3 RVLRLKAINRVPSMRILVNLLIDTLPMGNVLLLCFFVFFIFGIGVQLWAGLRLRNRCFLEENFTIQGDVA-LPPYYQPEEDEMPPFICSLTGDNIMG
 hCavT1a RVLRLKAINRVPSMRILVNLLIDTLPMGNVLLLCFFVFFIFGIGVQLWAGLRLRNRCFLEENFTIQGDVA-LPPYYQPEEDEMPPFICSLTGDNIMG
 rCavT1a RVLRLKAINRVPSMRILVNLLIDTLPMGNVLLLCFFVFFIFGIGVQLWAGLRLRNRCFLEENFTIQGDVA-LPPYYQPEEDEMPPFICSLTGDNIMG
 hCavT2a RVLRLKAINRVPSMRILVNLLIDTLPMGNVLLLCFFVFFIFGIGVQLWAGLRLRNRCFLEENFTIQGDVA-LPPYYQPEEDEMPPFICSLTGDNIMG
 hCavT3 RVLRLKAINRVPSMRILVNLLIDTLPMGNVLLLCFFVFFIFGIGVQLWAGLRLRNRCFLEENFTIQGDVA-LPPYYQPEEDEMPPFICSLTGDNIMG
 rCavT3 RVLRLKAINRVPSMRILVNLLIDTLPMGNVLLLCFFVFFIFGIGVQLWAGLRLRNRCFLEENFTIQGDVA-LPPYYQPEEDEMPPFICSLTGDNIMG
 hCavT1a LLIIVGSEFMINCLVVIATQFSETKORESQLMREQRVRFLSNASTLASFEPGSCYELLKYLVYILRKARRLAQVSRAAGVRLLSSPAPLGGQET
 rCavT1a LLIIVGSEFMINCLVVIATQFSETKORESQLMREQRVRFLSNASTLASFEPGSCYELLKYLVYILRKARRLAQVSRAIGVAGLISSPVARSQGP
 hCavT2a CSHIPGRDVRMPCTLGWEA-YTOPQA GVGAARNACINWNQYNNCRSGDSNPHNGAINFDNTCYAWIIFQVTLERHMLLEORQYLS-
 hCavT3 CHEIPPLKEQGRECCCLSKDVIDFGAGRODLNASGLCVNWNRYNNCRIGTSANPHKGAINFDNIGYAGIVIFQVTLERHMLLEORQYLS-
 rCavT3 CHEIPPLKEQGRECCCLSKDVIDFGAGRODLNASGLCVNWNRYNNCRIGTSANPHKGAINFDNIGYAGIVIFQVTLERHMLLEORQYLS-

Fig. 1A

hCavT1a QPSSCSRSHRRLSVHHLYHHHHHHHHHHHHHHLGNGTLRAPRASPEIQDORDANGSRRLMLPPSTPALSAGAPPGCA-----ESVHSEYHADCHLEPVRC
 rCavT1a QPSGSCTRSRRLSVHHLYHHHHHHHHHHHHHHLGNGTLRVPRASPEIQDORDANGSRRLMLPPSTPAPSQQPPRGA-----ESVHSEYHADCHLEPVRC
 hCavT2a GHQRAGRHTAVHHLYHYHFSHGSPRRGPPEPGACDTLVRAGAPPSSPPSGRPDAE-----SVHSIYHADCHIEGPOERARVGTCSRSHCRC
 hCavT3 -----
 rCavT3 -----
 rCavT3 -----

hCavT1a QAPPPRSPSEASGRRTVGSGKVYPTVHTSPPPETIKEKALVEVAASSCPPTILTSLN-IPPGPYSSMHKLLETQSTGACQSSCKISSPCLKA
 rCavT1a QAPPPRCPSSEASGRRTVGSGKVYPTVHTSPPPETIKEKALVEVAPSPPGPTILTSFN-IPPGPSSSMHKLLETQSTGACHSSCKISSPCSKA
 hCavT2a OPOAQRAGHHELPHDPALRGGORQROHQOPTQEGYGRWTARHRHGHPLSLNSPDPYKEKIPHVAGEHGLQAPGHLSSGLSVPCPLPSPPAGT
 hCavT3 -----
 rCavT3 -----
 rCavT3 -----

hCavT1a PYCARA-GAGEVELADREMPDSDEAVYEFTQDAQHSDLRDPHS-----RR-QRSILGPDAEPSSVLAFWRLICDTFRKIVDVKSYFGRGIM
 rCavT1a PYCART-GAGEPESDHVMMPDSDEAVYEFTQDAQHSDLRDPHS-----RRRQRSILGPDAEPSSVLAFWRLICDTFRKIVDVKSYFGRGIM
 hCavT2a PYCTRaledPECELSGSSESGDSDGRGVYEFQDVRHGDWRDPTRPRPA-----TPGPGPSQRRQAAPGEPGWMGRLMWTFSGKLRRIVDSKYF
 hCavT3 PCQHEDGRRPSGLGSTSQEGS-----GCSSSAGGEEADGDGARSEDGASSELGKEEEEEEQADGAVWLCCDVMRETRAKLRGIVDVKSYFNRGIM
 rCavT3 PHCQHEAGRPSGLGSTSQEGS-----GGSSA-EAEANGDGLOSSEDGVSSDLGKEEQE---DGAARLICGDDWRETRKLRGIVDVKSYFNRGIM

IIS1 -----
 hCavT1a IAILVNTLSMGIYHEQPEELTNALEISNIVETSLFIALEMILKLVYGFEGYTKNPYNIFDGVIVVVISWEIVGQQQGGGLSVLRTFRMRVILKLVRF
 rCavT1a IAILVNTLSMGIYHEQPEELTNALEISNIVETSLFIALEMILKLVYGFEGYTKNPYNIFDGVIVVVISWEIVGQQQGGGLSVLRTFRMRVILKLVRF
 hCavT2a MAILVNTLSMGIYHEQPEELTNALEISNIVETSMFALEMILKLVYGFEGYTKNPYNIFDGVIVVVISWEIVGQQADGGLSVLRTFRMRVILKLVRF
 hCavT3 MAILVNTVSMGIYHEQPEELTNILEICNVVFTSMFALEMILKLAAGFLFDYLRNPNINFDSIVIVISWEIVGQADGGLSVLRTFRMRVILKLVRF
 rCavT3 MAILVNTVSMGIYHEQPEELTNILEICNVVFTSMFALEMILKLAAGFLFDYLRNPNINFDSIVIVISWEIVGQADGGLSVLRTFRMRVILKLVRF

IIS2 -----
 hCavT1a IAILVNTLSMGIYHEQPEELTNALEISNIVETSLFIALEMILKLVYGFEGYTKNPYNIFDGVIVVVISWEIVGQQQGGGLSVLRTFRMRVILKLVRF
 rCavT1a IAILVNTLSMGIYHEQPEELTNALEISNIVETSLFIALEMILKLVYGFEGYTKNPYNIFDGVIVVVISWEIVGQQQGGGLSVLRTFRMRVILKLVRF
 hCavT2a MAILVNTLSMGIYHEQPEELTNALEISNIVETSMFALEMILKLVYGFEGYTKNPYNIFDGVIVVVISWEIVGQQADGGLSVLRTFRMRVILKLVRF
 hCavT3 MAILVNTVSMGIYHEQPEELTNILEICNVVFTSMFALEMILKLAAGFLFDYLRNPNINFDSIVIVISWEIVGQADGGLSVLRTFRMRVILKLVRF

IIS3 -----
 hCavT1a IAILVNTLSMGIYHEQPEELTNALEISNIVETSLFIALEMILKLVYGFEGYTKNPYNIFDGVIVVVISWEIVGQQQGGGLSVLRTFRMRVILKLVRF
 rCavT1a IAILVNTLSMGIYHEQPEELTNALEISNIVETSLFIALEMILKLVYGFEGYTKNPYNIFDGVIVVVISWEIVGQQQGGGLSVLRTFRMRVILKLVRF
 hCavT2a MAILVNTLSMGIYHEQPEELTNALEISNIVETSMFALEMILKLVYGFEGYTKNPYNIFDGVIVVVISWEIVGQQADGGLSVLRTFRMRVILKLVRF
 hCavT3 MAILVNTVSMGIYHEQPEELTNILEICNVVFTSMFALEMILKLAAGFLFDYLRNPNINFDSIVIVISWEIVGQADGGLSVLRTFRMRVILKLVRF

IIP LOOP -----
 hCavT1a LQRQLVVLMKITMDNVATFCMILMIFIFISLGMHILFGCKFASERD-GDTLPDRKNFDSLWIAIVTVFQILTQEDWKVLYNGMASTSSWA
 rCavT1a LQRQLVVLMKITMDNVATFCMILMIFIFISLGMHILFGCKFASERD-GDTLPDRKNFDSLWIAIVTVFQILTQEDWKVLYNGMASTSSWA
 hCavT2a LRRQLVVLVKTMDNVATFCMILMIFIFISLGMHIFGCKFSLKTDGDTVPDRKNFDSLWIAIVTVFQILTQEDWNVLYNGMASTSSWA
 hCavT3 LRRQLVVLVKTMDNVATFCMILMIFIFISLGMHIFGCKFSLRTDGTVPDRKNFDSLWIAIVTVFQILTQEDWNVLYNGMASTSPWA
 rCavT3 LRRQLVVLVKTMDNVATFCMILMIFIFISLGMHIFGCKFSLRTDGTVPDRKNFDSLWIAIVTVFQILTQEDWNVLYNGMASTTPWA

Fig. 1B

IIIS6

hCavT1a FGNYVLFNLLVAILVEGFFQAEGDANKSESEPDEFFSPSLDGDGRKKCLALVSLGEHPELRKSLLPPL-----IHTAAATPMSSLPKSTSTGLGEALGPASR
 rCavT1a FGNYVLFNLLVAILVEGFFQAEGDATKSESEPDEFFSPSVDPGDGRKKCLALVALGEHAELRKSLLPPL-----IHTAAATPMSPHKSSSTGVCGEALGSRR
 hCavT1a FGNYVLFNLLVAILVEGFFQAEGDANRSDTDEDTKSYHFEEDFHKLRELOTTELKMCSLAVTENGTRDEAACPLPSSCAQLPRPCLPPRAHSWMOPPAS
 hCavT3 FGNYVLFNLLVAILVEGFFQAEGDANRSYSDQDQSSNTIEFDKLOEGLDSSGDPRLCPIPMTPNGLDPSLPIGGHLGPAGAAGPAPRLSLOPDPMVLVAL
 rCavT3 FGNYVLFNLLVAILVEGFFQAEGDANRSCSDQDQSSNLLEFDKLPEGLDNSRDLKLCPIPMTPNGLDPSLPLGAHLGPAGTMGTAPRLSLOPDPMVLVAL

hCavT1a RTSSSGSAEPGAAH-EMKSPPSARSSPHSPWSAASSWTSSRSSRNLSLGRAPSILKRR-----SPSGERRSLLSGEQESQDEEESEEERASP
 rCavT1a RTSSSGSAEPGAAHHEMCKPPSARSSPHSPWSAASSWTSSRSSRNLSLGRAPSILKRR-----SPSGERRSLLSGEQESQDEEESEEERASP
 hCavT2a QTLGVAAAAPGTRHWETRSLRQPPKFSLCPLGPSCAWSSSSWSSSLIGRAQPO-----PACOCGERESESSLSGKGSTTDDEAEDGRARS
 hCavT3 GSRKSSVMISLGMSYDQRSLSSSSSSYYGPWGWSAAAWSRRSSWNSSLKHKPPSAEHESLSSAERGGG-ARVCEVAADEGPPRAAPLHTPAHNVHHGPHL
 rCavT3 DSRKSSVMISLGMSYDQRSLSSSSSSYYGPWGWSGTWASSRRSSWNSSLKHKPPSAEHESLSSCEGGGSCVRAZEGAREEAPTRTAPLHAPHAAHHGPHL

hCavT1a AGSDHRHRCGSLEREAKSFIDLPTDLQVPGLHRTASGRGSAEH--ODCNGKSAAGRGLARALRFDDPPLDGDADDEGNLSKGERVRAWIRARLPACCLERD
 rCavT1a AGSDHRHRCGSLEREAKSFIDLPTDLQVPGLHRTASGRGSAEH--ODCNGKSAAGRGLARLTLLTDDPQLDGDDDNDEGNLSKGERVIAWVRSRLPACCRERD
 hCavT2a GPRATPLRRAESLDRP-----PLRRPPPAYQVRDRDGQVYALPSDFFLRIDSHREDAAELODDSEDSCCCLRLHKVLPYKQPQRCSRSPRG
 hCavT3 AHRHRHHRRTLSLDNRDSVDLAELVPAVGAHPRAAWRAAGAPGHEDCNGRMPMSIAKDVFTKMGDRGDREDEEEIDYTLCFVRKMDIVYKPDWCEVRE
 rCavT3 AHRHRHHRRTLSLDTRDSVDLGELYPVVGAHSRAAMRGAGQAPGHEDCNGRMPNIAKDVFTKMDDRRDGEDEEEIDYTLCFVRKMDIVYKPDWCEVRE

IIIS1

hCavT1a SWAYIFPPQSFRILLCHRILTHQFDHVVLVILFNCNTIAMERPKIDPHSAERIFLTLSNVIIFTAVFLAEMTVKVKYALGWCFGEQAYLRSWNVLDDGL
 rCavT1a SWAYIFPPQSFRILLCHRILTHQFDHVVLVILFNCNTIAMERPKIDPHSAERIFLTLSNVIIFTAVFLAEMTVKVKYALGWCFGEQAYLRSWNVLDDGL
 hCavT2a PSTLYLFSPONRFRVSCQVITHQFDHVVLVILFNCNTIAMERPKIDPGSTERVFLSNSNVIIFTAIFVAEMMVKVKYALGLISGEHAYLQSSWNLLDGF
 hCavT3 DWSVYLFSPENRFRVLCQITIAHKLFDYVVLAFNLCNTIALERPQIEAGSTERIFLTVSNSNVIIFTAIFVGEMTLKVSLGLYFGEQAYLRSWNVLDDGF
 rCavT3 DWSVYLFSPENKFRILCQITIAHKLFDYVVLAFNLCNTIALERPQIEAGSTERIFLTVSNSNVIIFTAIFVGEMTLKVSLGLYFGEQAYLRSWNVLDDGF

IIIS3

hCavT1a LVLLISVIDILVSMVSDSGTKILGMRLVRLRPLRVISRAQGLKLVVTIMSSLKPIGNIVVTCACAFFIIFGIGLGVQLFKGKFFFCQGEDTRNITNK
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 hCavT2a LVLLISVIDILVSMVSDSGTKILGMRLVRLRPLRVISRAQGLKLVVTIMSSLKPIGNIVVTCACAFFIIFGIGLGVQLFKGKFFFCQGEDTRNITNK
 hCavT3 LVFVSIIDIVVSLASAGGAKILGVRLVRLRPLRVISRAQGLKLVVTIMSSLKPIGNIVVTCACAFFIIFGIGLGVQLFKGKFFFCQGEDTRNITNK
 rCavT3 LVFVSIIDIVVSLASAGGAKILGVRLVRLRPLRVISRAQGLKLVVTIMSSLKPIGNIVVTCACAFFIIFGIGLGVQLFKGKFFFCQGEDTRNITNK

Fig. 1C

Fig. 1D

hCa_vT1a SYMCRHGSTAEGPLGHRGWGLPKAQSGCSVLSVHSQPADTSYILQLPKDAPHLLQFHSAPTWGGTIPKLPPPGRSPLAQRLRRQAIRTDSDLVQGLGSRE
 rCa_vT1a SYMCRNGSTAIERSLGHRGWGLPKAQSGSISILSVHSQADTSCLQLPKDVHYLLQPHGAPTGAIPKLPPGRSPLAQRLRRQAIRTDSDLVQGLGSRE
 hCa_vT2a SYMERTPVPVAPASAPHBRPLOEVEMETYGACTPLGSVASVHSSPAE SCASLQIPLAVSSPARSE-----
 hCa_vT3 -----GPRLIPTGSPGAPGRGGAGGGDTDGGLCRRCYSPAQNWLDSVSLLIKDS-----
 rCa_vT3 -----GPRLIPTSSPGAPGRGGAGGGDTESHLRHCYSPAETLWLDSVSLLIKDS-----
 hCa_vT1a DLIAEVSGPSPLARAYSTFWGQSSTTAQQHSHSKISKHMTPPAPCPGPEPNWGKGPPETRSSLLELDTELSWISGDLILPPGGQEEPPSPRDLKKCYSV
 rCa_vT1a DLISEVSGPSCPTRSSFWGSSIQVQQRSGIQSKVSKHIRLPAPCPGLEPSWAKDOPPETRSSLLELDTELSWISGDLILPPSS-QEEPLFPDRDLKKCYSV
 hCa_vT2a -----PLHALSPRGTTARSPLSRLLCRQEAVHTDSLKGRLTAIGTPWILQSLVRKPR (SEQ ID NO: 9)
 hCa_vT3 -----LEGELTIIDNLSGSIFHHYSSPAGCKKHHDKQETGPRPSCWTII (SEQ ID NO: 11)
 rCa_vT3 -----LEGELTIIDNLSGSVEFHHYASPDGCGKCHHDKQETGLHPSCWMT (SEQ ID NO: 12)
 hCa_vT1a AOSCORRPTSWLDEQRRIHSIAVSCLDSGSQPHLGTDPNSNIGGQPLGGPSRKPKKLSSPPSITIDPPESQGPRTPPSPGICLRRRAPSSDSKDPDPLASGPPD
 rCa_vT1a TQSCRERRPGFWLDEQRRIHSIAVSCLDSGSQPRLCPSSSILGGQPLGGPSRKPKKLSSPPSISIDPPESQGSRRPCSPGVCLRRRAPASDSKDPDPSVSSPLD
 hCa_vT1a SMAASPSPKKDVLSLGCLSSDPADLDP (SEQ ID NO: 1)
 rCa_vT1a STAASPSPKKKDTLISLGCLSSDPDMDP (SEQ ID NO: 5)

Fig. 1E

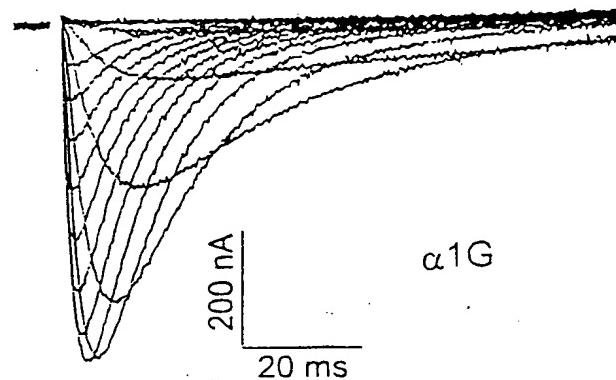


Figure 2A

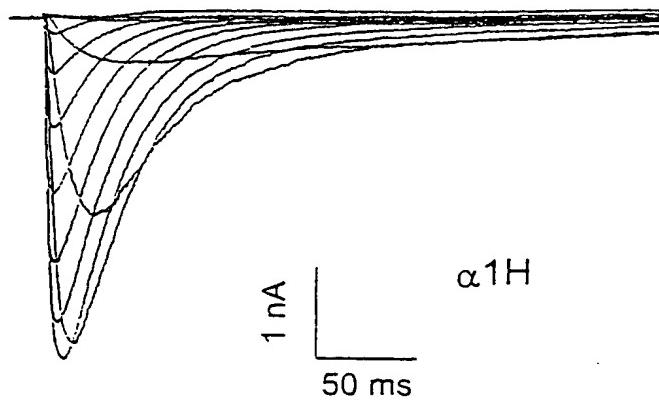


Figure 2B

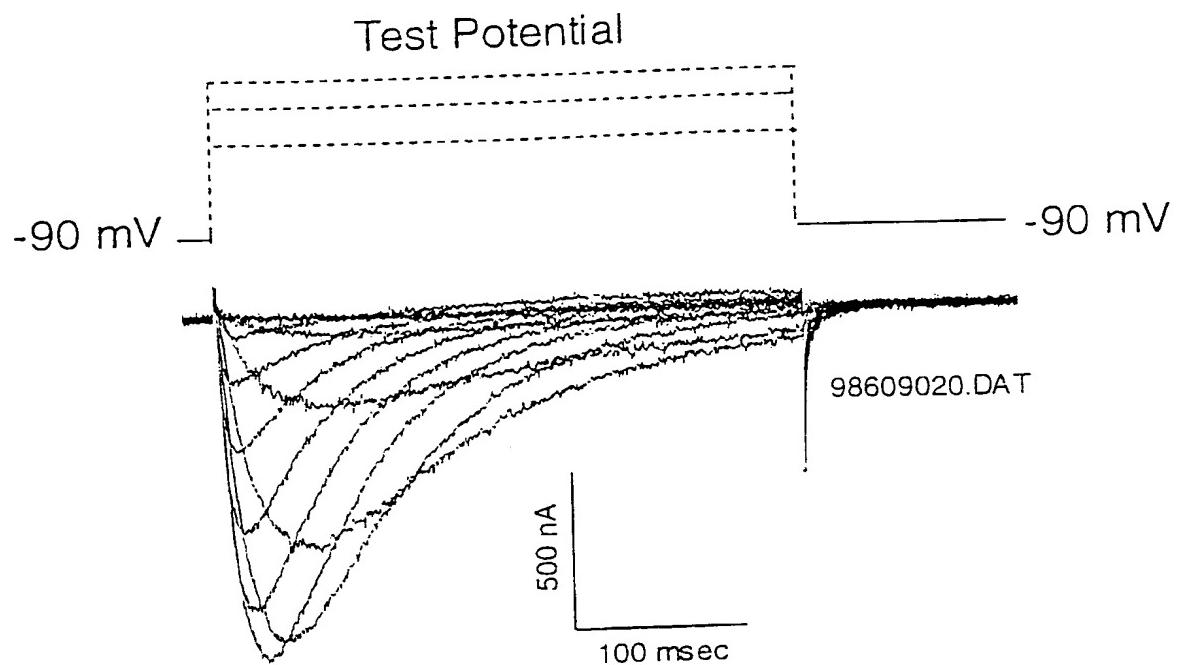


Figure 2C

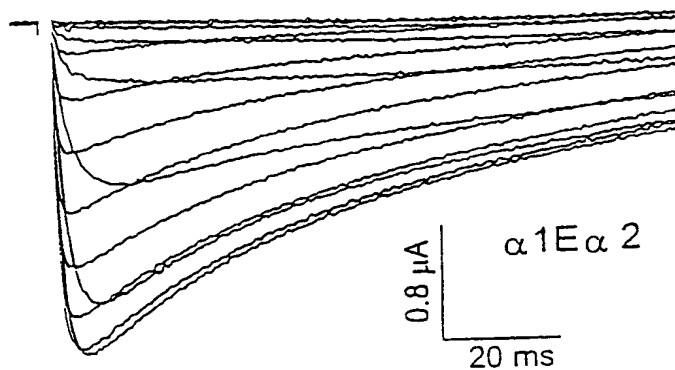
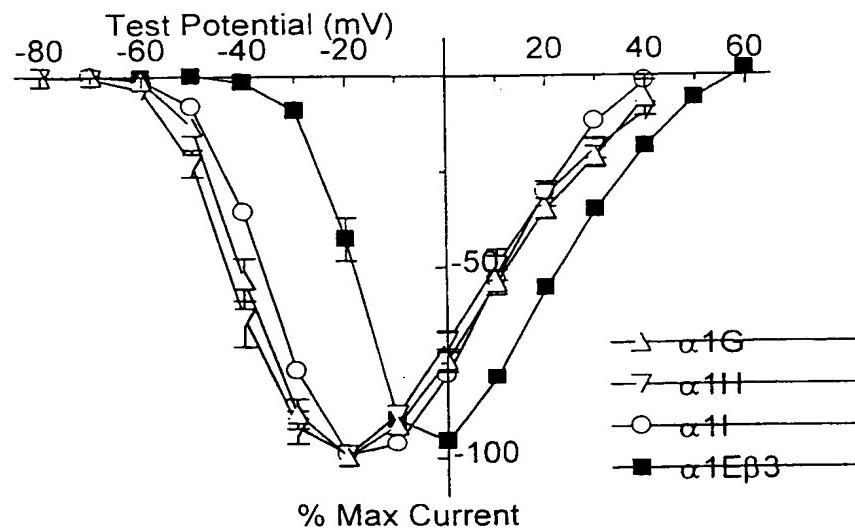
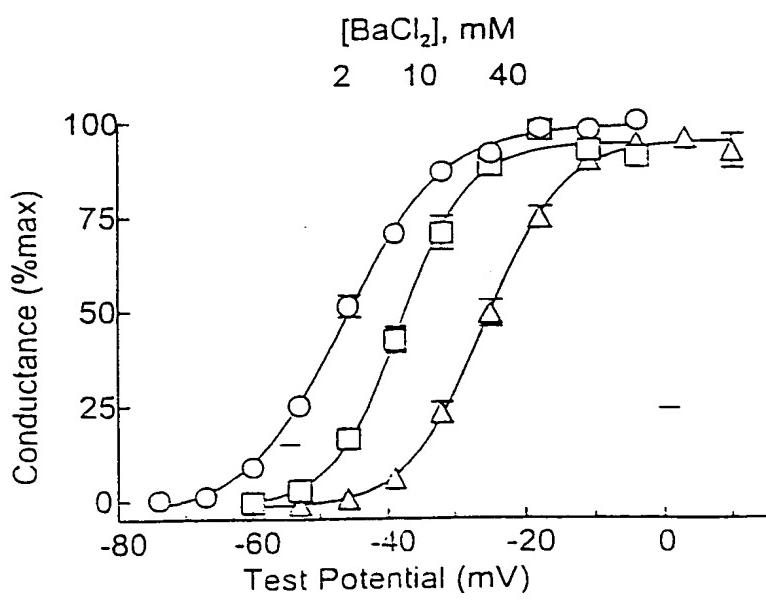


Figure 2D

**Figure 3A****Figure 3B**

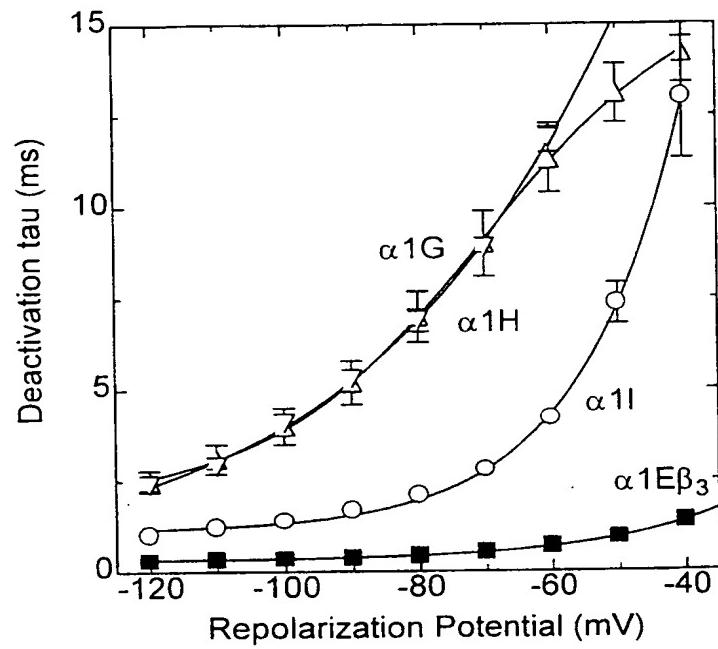


Figure 4

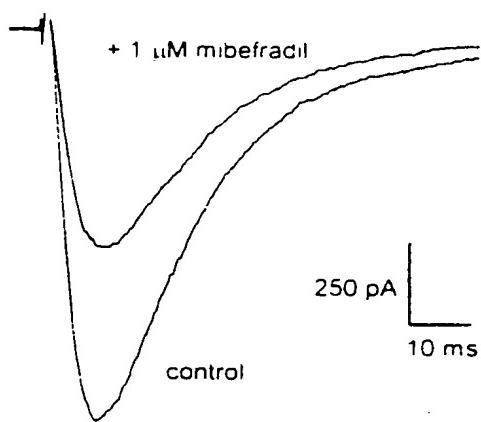


Figure 5A

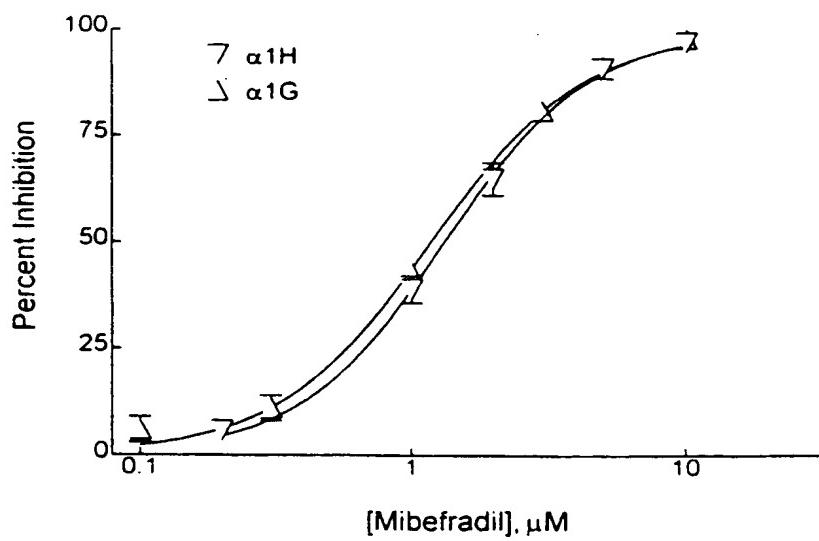


Figure 5B

SEQUENCE LISTING

5 <110> Perez-Reyes, Edward
 Cribbs, Leanne L.
 Loyola University of Chicago

10 <120> T-TYPE VOLTAGE-GATED CALCIUM CHANNELS AND METHOD OF
 USING SAME

15 <130> 89066

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25 <150> US 08/985,809
 <151> 1997-12-05

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35 <170> PatentIn Ver. 2.0

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65 ggg ccg ggg tca gca gaa aag gac ccg ggc agc gcg gac tcc gag gcg Gly Pro Gly Ser Ala Glu Lys Asp Pro Gly Ser Ala Asp Ser Glu Ala 35 40 45	144
70 gag ggg ctg ccg tac ccg gcg ctg gcc ccg gtg gtt ttc ttc tac ttg Glu Gly Leu Pro Tyr Pro Ala Leu Ala Pro Val Val Phe Phe Tyr Leu 50 55 60	192
75 agc cag gac agc cgc ccg cgg agc tgg tgt ctc cgc acg gtc tgt aac Ser Gln Asp Ser Arg Pro Arg Ser Trp Cys Leu Arg Thr Val Cys Asn 65 70 75 80	240
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85 acc ctg ggc atg ttc cgg cca tgc gag gac atc gcc tgt gac tcc cag Thr Leu Gly Met Phe Arg Pro Cys Glu Asp Ile Ala Cys Asp Ser Gln 100 105 110	336
90 cgc tgc cgg atc ctg cag gcc ttt gat gac ttc atc ttt gcc ttc ttt Arg Cys Arg Ile Leu Gln Ala Phe Asp Asp Phe Ile Phe Ala Phe Phe 115 120 125	384
95 gcc gtg gag atg gtg gtg aag atg gtg gcc ttg ggc atc ttt ggg aaa	432

	Ala Val Glu Met Val Val Lys Met Val Ala Leu Gly Ile Phe Gly Lys	
	130 135 140	
5	aag tgt tac ctg gga gac act tgg aac cgg ctt gac ttt ttc atc gtc Lys Cys Tyr Leu Gly Asp Thr Trp Asn Arg Leu Asp Phe Phe Ile Val	480
	145 150 155 160	
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	165 170 175	
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	180 185 190	
20	cgg gtg ccc agc atg cgc atc ctt gtc acg ttg ctg gat acg ctg Arg Val Pro Ser Met Arg Ile Leu Val Thr Leu Leu Asp Thr Leu	624
	195 200 205	
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	210 215 220	
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	245 250 255	
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	260 265 270	
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	355 360 365	
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	405 410 415	
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	420 425 430	
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	450 455 460	
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	465 470 475 480	
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	485 490 495	
30	cac cac cac cat cac cac tac cac ctg ggc aat ggg acg ctc His His His His His His Tyr His Leu Gly Asn Gly Thr Leu	1536
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	515 520 525	
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	545 550 555 560	
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	565 570 575	
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	580 585 590	
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	595 600 605	
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	610 615 620	
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20	ctc cgg gac ccc cac agc cgg cgg caa cgg agc ctg ggc cca gat gca Leu Arg Asp Pro His Ser Arg Arg Gln Arg Ser Leu Gly Pro Asp Ala	705 710 715	2160
25	720		
25	gag ccc agc tct gtg ctg gcc ttc tgg agg cta atc tgt gac acc ttc Glu Pro Ser Ser Val Leu Ala Phe Trp Arg Leu Ile Cys Asp Thr Phe	725 730 735	2208
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30	750		
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45	ctc ttt gcc ctg gag atg ctg ctg aag ctg ctt gtg tat ggt ccc ttt Leu Phe Ala Leu Glu Met Leu Leu Lys Leu Val Tyr Gly Pro Phe	785 790 795	2400
45	795 800		
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50	815		
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65	875 880		
60	atc ctg ggc atg cat ctc ttc ggc tgc aag ttt gcc tct gag cgg gat Ile Leu Gly Met His Leu Phe Gly Cys Lys Phe Ala Ser Glu Arg Asp	885 890 895	2688
60	895		
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	Gly Asp Thr Leu Pro Asp Arg Lys Asn Phe Asp Ser Leu Leu Trp Ala	
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10	ctc tac aat ggt atg gcc tcc ac ^g tcg tcc tgg gc ^g gcc ctt tat ttc Leu Tyr Asn Gly Met Ala Ser Thr Ser Trp Ala Ala Leu Tyr Phe 930 935 940	2332
15	att gcc ctc atg acc ttc ggc aac tac gtg ctc ttc aat ttg ctg gtc Ile Ala Leu Met Thr Phe Gly Asn Tyr Val Leu Phe Asn Leu Leu Val 945 950 955 960	2880
20	gcc att ctg gtg gag ggc ttc cag gc ^g gag gga gat gcc aac aag tcc Ala Ile Leu Val Glu Gly Phe Gln Ala Glu Gly Asp Ala Asn Lys Ser 965 970 975	2928
25	gaa tca gag ccc gat ttc ttc tca ccc agc ctg gat ggt gat ggg gac Glu Ser Glu Pro Asp Phe Ser Pro Ser Leu Asp Gly Asp Gly Asp 980 985 990	2976
30	agg aag aag tgc ttg gcc ttg gtg tcc ctg gga gag cac ccg gag ctg Arg Lys Lys Cys Leu Ala Leu Val Ser Leu Gly Glu His Pro Glu Leu 995 1000 1005	3024
35	cg ^g aag agc ctg ctg cc ^g cct ctc atc atc cac ac ^g gc ^c gc ^c aca ccc Arg Lys Ser Leu Leu Pro Pro Leu Ile Ile His Thr Ala Ala Thr Pro 1010 1015 1020	3072
40	atg tcg ctg ccc aag agc acc agc ac ^g ggc ctg ggc gag gc ^g ctg ggc Met Ser Leu Pro Lys Ser Thr Ser Thr Gly Leu Gly Glu Ala Leu Gly 1025 1030 1035 1040	3120
45	cct gc ^g tcg cg ^c cg ^c acc agc agc gg ^g tcg gca gag cct gg ^g gc ^g Pro Ala Ser Arg Arg Thr Ser Ser Gly Ser Ala Glu Pro Gly Ala 1045 1050 1055	3168
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55	ccc tgg agc gct gca agc agc tgg acc agc agg cg ^c tcc agc cg ^g aac Pro Trp Ser Ala Ala Ser Ser Trp Thr Ser Arg Arg Ser Ser Arg Asn 1075 1080 1085	3264
60	agc ctc ggc cgt gca ccc agc ctg aag cg ^g aga agc cca agt gga gag Ser Leu Gly Arg Ala Pro Ser Leu Lys Arg Arg Ser Pro Ser Gly Glu 1090 1095 1100	3312
65	cg ^g cg ^g tcc ctg ttg tcg gga gaa gg ^c cag gag agc cag gat gaa gag Arg Arg Ser Leu Leu Ser Gly Glu Gly Gln Glu Ser Gln Asp Glu Glu 1105 1110 1115 1120	3360
70	gag agc tca gaa gag gag cg ^c gcc agc cct gc ^c gg ^c agt gac cat cg ^c Glu Ser Ser Glu Glu Glu Arg Ala Ser Pro Ala Gly Ser Asp His Arg 1125 1130 1135	3408
75	cac agg ggg tcc ctg gag cg ^c gag gg ^c aag agt tcc ttt gac ctg cca His Arg Gly Ser Leu Glu Arg Glu Ala Lys Ser Ser Phe Asp Leu Pro 1140 1145 1150	3456
	gac aca ctg cag gtg cca gg ^c ctg cat cg ^c act gc ^c agt gg ^c cg ^a gg ^c	3504

	Asp Thr Leu Gln Val Pro Gly Leu His Arg Thr Ala Ser Gly Arg Gly		
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5	tct gct tct gag cac cag gac tgc aat ggc aag tcg gct tca ggg cgc	3552	
	Ser Ala Ser Glu His Gln Asp Cys Asn Gly Lys Ser Ala Ser Gly Arg		
	1170	1175	1180
10	ctg gcc cgccgtcgatgaccccctgatggggatgac	3600	
	Leu Ala Arg Ala Leu Arg Pro Asp Asp Pro Pro Leu Asp Gly Asp Asp		
	1185	1190	1195
	1200		
	gcc gat gac gag ggc aac ctg agc aaa ggg gaa cgg gtc cgc gcg tgg	3648	
	Ala Asp Asp Glu Gly Asn Leu Ser Lys Gly Glu Arg Val Arg Ala Trp		
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15	atc cga gcc cga ctc cct gcc tgc tgc ctc gag cga gac tcc tgg tca	3696	
	Ile Arg Ala Arg Leu Pro Ala Cys Cys Leu Glu Arg Asp Ser Trp Ser		
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20	gcc tac atc ttc cct cag tcc agg ttc cgc ctc ctg tgt cac cgg	3744	
	Ala Tyr Ile Phe Pro Pro Gln Ser Arg Phe Arg Leu Leu Cys His Arg		
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25	atc atc acc cac aag atg ttc gac cac gtg gtc ctt gtc atc atc ttc	3792	
	Ile Ile Thr His Lys Met Phe Asp His Val Val Leu Val Ile Ile Phe		
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30	ctt aac tgc atc acc atc gcc atg gag cgc ccc aaa att gac ccc cac	3840	
	Leu Asn Cys Ile Thr Ile Ala Met Glu Arg Pro Lys Ile Asp Pro His		
	1265	1270	1275
	1280		
	agc gct gaa cgc atc ttc ctg acc ctc tcc aat tac atc ttc acc gca	3888	
	Ser Ala Glu Arg Ile Phe Leu Thr Leu Ser Asn Tyr Ile Phe Thr Ala		
	1285	1290	1295
35	gtc ttt ctg gct gaa atg aca gtg aag gtg gtg gca ctg ggc tgg tgc	3936	
	Val Phe Leu Ala Glu Met Thr Val Lys Val Val Ala Leu Gly Trp Cys		
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40	ttc ggg gag cag gcg tac ctg cgg agc agt tgg aac gtg ctg gac ggg	3984	
	Phe Gly Glu Gln Ala Tyr Leu Arg Ser Ser Trp Asn Val Leu Asp Gly		
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45	ctg ttg gtg ctc atc tcc gtc atc gac att ctg gtg tcc atg gtc tct	4032	
	Leu Leu Val Leu Ile Ser Val Ile Asp Ile Leu Val Ser Met Val Ser		
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50	gac agc ggc acc aag atc ctg ggc atg ctg agg gtg ctg cgg ctg ctg	4080	
	Asp Ser Gly Thr Lys Ile Leu Gly Met Leu Arg Val Leu Arg Leu Leu		
	1345	1350	1355
	1360		
	cgg acc ctg cgc ccg ctc agg gtg atc agc cgg gcg cag ggg ctg aag	4128	
	Arg Thr Leu Arg Pro Leu Arg Val Ile Ser Arg Ala Gln Gly Leu Lys		
	1365	1370	1375
55	ctg gtg gtg gag acg ctg atg tcc tca ctg aaa ccc atc ggc aac att	4176	
	Leu Val Val Glu Thr Leu Met Ser Ser Leu Lys Pro Ile Gly Asn Ile		
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60	gta gtc atc tgc tgt gcc ttc ttc att ttc ggc atc ttg ggg gtg	4224	
	Val Val Ile Cys Cys Ala Phe Phe Ile Ile Phe Gly Ile Leu Gly Val		
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	cag ctc ttc aaa ggg aag ttt ttc gtg tgc cag ggc gag gat acc agg	4272	

	Gln Leu Phe Lys Gly Lys Phe Phe Val Cys Gln Gly Glu Asp Thr Arg		
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	1425 1430 1435 1440		
10	cgg cac aag tac aac ttt gac aac ctt ggc cag gcc ctg atg tcc ctg Arg His Lys Tyr Asn Phe Asp Asn Leu Gly Gln Ala Leu Met Ser Leu		4368
	1445 1450 1455		
15	ttc gtt ttg gcc tcc aag gat ggt tgg gtg gac atc atg tac gat ggg Phe Val Leu Ala Ser Lys Asp Gly Trp Val Asp Ile Met Tyr Asp Gly		4416
	1460 1465 1470		
	ctg gat gct gtg ggc gtg gac cag cag ccc atc atg aac cac aac ccc Leu Asp Ala Val Gly Val Asp Gln Gln Pro Ile Met Asn His Asn Pro		4464
	1475 1480 1485		
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	1490 1495 1500		
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	1505 1510 1515 1520		
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	1525 1530 1535		
	cta cga aga ctg gag aaa aag aga agg agt aag gag aag cag atg gct Leu Arg Arg Leu Glu Lys Lys Arg Arg Ser Lys Glu Lys Gln Met Ala		4656
35	1540 1545 1550		
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	1555 1560 1565		
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	1570 1575 1580		
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	1585 1590 1595 1600		
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	1605 1610 1615		
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55	1620 1625 1630		
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	1635 1640 1645		
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	1650 1655 1660		
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	Ala Ser Leu Pro Ile Asn Pro Thr Ile Ile Arg Ile Met Arg Val Leu		
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	1685 1690 1695		
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	1700 1705 1710		
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	1715 1720 1725		
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	1730 1735 1740		
25	ctg ggc cgt cat gcc acc ttt cgg aac ttt ggc atg gcc ttc cta acc Leu Gly Arg His Ala Thr Phe Arg Asn Phe Gly Met Ala Phe Leu Thr		5280
	1745 1750 1755 1760		
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	1765 1770 1775		
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	1780 1785 1790		
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	1795 1800 1805		
45	gtc aac gtg gtg atc gcc gtg ctg atg aag cac ctg gag gag agc aac Val Asn Val Val Ile Ala Val Leu Met Lys His Leu Glu Glu Ser Asn		5472
	1810 1815 1820		
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	1825 1830 1835 1840		
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	1845 1850 1855		
60	atc tgg cct ggg gtc gag ggc ccc gac agc ccc gac agc ccc aag cct Leu Trp Pro Gly Val Glu Gly Pro Asp Ser Pro Asp Ser Pro Lys Pro		5616
	1860 1865 1870		
65	ggg gct ctg cac cca gcg gcc cac gcg aga tca gcc tcc cac ttt tcc Gly Ala Leu His Pro Ala Ala His Ala Arg Ser Ala Ser His Phe Ser		5664
	1875 1880 1885		
70	ctg gag cac ccc acg atg cag ccc cac ccc acg gag ctg cca gga cca Leu Glu His Pro Thr Met Gln Pro His Pro Thr Glu Leu Pro Gly Pro		5712
	1890 1895 1900		
75	gac tta ctg act gtg cggt aag tct ggg gtc agc cga acg cac tct ctg Asp Leu Leu Thr Val Arg Lys Ser Gly Val Ser Arg Thr His Ser Leu		5760
	1905 1910 1915 1920		
	ccc aat gac agc tac atg tgt cgg cat ggg agc act gcc gag ggg ccc		5808

	Pro Asn Asp Ser Tyr Met Cys Arg His Gly Ser Thr Ala Glu Gly Pro		
	1925	1930	1935
5	ctg gga cac agg ggc tgg ggg ctc ccc aaa gct cag tca ggc tcc gtc Leu Gly His Arg Gly Trp Gly Leu Pro Lys Ala Gin Ser Gly Ser Val		5556
	1940	1945	1950
10	ttg tcc gtt cac tcc cag cca gca gat acc agc tac atc ctg cag ctt Leu Ser Val His Ser Gln Pro Ala Asp Thr Ser Tyr Ile Leu Gln Leu		5904
	1955	1960	1965
	ccc aaa gat gca cct cat ctg ctc cag ccc cac agc gcc cca acc tgg Pro Lys Asp Ala Pro His Leu Leu Gln Pro His Ser Ala Pro Thr Trp		5952
15	1970	1975	1980
	ggc acc atc ccc aaa ctg ccc cca cca gga cgc tcc cct ttg gct cag Gly Thr Ile Pro Lys Leu Pro Pro Gly Arg Ser Pro Leu Ala Gln		6000
	1985	1990	1995
20	agg cca ctc agg cgc cag gca gca ata agg act gac tcc ttg gac gtt Arg Pro Leu Arg Arg Gln Ala Ala Ile Arg Thr Asp Ser Leu Asp Val		6048
	2005	2010	2015
25	cag ggt ctg ggc agc cgg gaa gac ctg ctg gca gag gtg agt ggg ccc Gln Gly Leu Gly Ser Arg Glu Asp Leu Leu Ala Glu Val Ser Gly Pro		6096
	2020	2025	2030
30	tcc ccg ccc ctg gcc cgg gcc tac tct ttc tgg ggc cag tca agt acc Ser Pro Pro Leu Ala Arg Ala Tyr Ser Phe Trp Gly Gln Ser Ser Thr		6144
	2035	2040	2045
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35	2050	2055	2060
	acc ccg cca gcc cct tgc cca ggc cca gaa ccc aac tgg ggc aag ggc Thr Pro Pro Ala Pro Cys Pro Gly Pro Glu Pro Asn Trp Gly Lys Gly		6240
	2065	2070	2075
40	cct cca gag acc aga agc agc tta gag ttg gac acg gag ctg agc tgg Pro Pro Glu Thr Arg Ser Ser Leu Glu Leu Asp Thr Glu Leu Ser Trp		6288
	2085	2090	2095
45	att tca gga gac ctc ctg ccc cct ggc ggc cag gag gag ccc cca tcc Ile Ser Gly Asp Leu Leu Pro Pro Gly Gly Gln Glu Pro Pro Ser		6336
	2100	2105	2110
50	cca cgg gac ctg aag aag tgc tac agc gtg gag gcc cag agc tgc cag Pro Arg Asp Leu Lys Lys Cys Tyr Ser Val Glu Ala Gln Ser Cys Gln		6384
	2115	2120	2125
	cgc cgg cct acg tcc tgg ctg gat gag cag agg aga cac tct atc gcc Arg Arg Pro Thr Ser Trp Leu Asp Glu Gln Arg Arg His Ser Ile Ala		6432
55	2130	2135	2140
	gtc agc tgc ctg gac agc ggc tcc caa ccc cac ctg ggc aca gac ccc Val Ser Cys Leu Asp Ser Gly Ser Gln Pro His Leu Gly Thr Asp Pro		6480
	2145	2150	2155
60	tct aac ctt ggg ggc cag cct ctt ggg ggg cct ggg agc cgg ccc aag Ser Asn Leu Gly Gln Pro Leu Gly Gly Pro Gly Ser Arg Pro Lys		6528
	2165	2170	2175
	aaa aaa ctc agc ccg cct agt atc acc ata gac ccc ccc gag agc caa		6576

	Lys Lys Leu Ser Pro Pro Ser Ile Thr Ile Asp Pro Pro Glu Ser Gln	
	2180 2185 2190	
5	ggt cct ccg acc ccg ccc agc cct ggt atc tgc ctc ccg agg agg gct Gly Pro Arg Thr Pro Pro Ser Pro Gly Ile Cys Leu Arg Arg Arg Ala	6624
	2195 2200 2205	
10	ccg tcc agc gac tcc aag gat ccc ttg gcc tct ggc ccc cct gac agc Pro Ser Ser Asp Ser Lys Asp Pro Leu Ala Ser Gly Pro Pro Asp Ser	6672
	2210 2215 2220	
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	1 5 10 15	
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	20 25 30	
40	ggg ccg ggg tca gca gaa aag gac ccg ggc agc gcg gac tcc gag gc ^g Gly Pro Gly Ser Ala Glu Lys Asp Pro Gly Ser Ala Asp Ser Glu Ala	144
	35 40 45	
45	gag ggg ctg ccg tac ccg gc ^g ctg gcc ccg gtg gtt ttc ttc tac ttg Glu Gly Leu Pro Tyr Pro Ala Leu Ala Pro Val Val Phe Phe Tyr Leu	192
	50 55 60	
50	agc cag gac agc ccg ccg agc tgg tgt ctc cgc acg gtc tgt aac Ser Gln Asp Ser Arg Pro Arg Ser Trp Cys Leu Arg Thr Val Cys Asn	240
	65 70 75 80	
55	ccc tgg ttt gag cgc atc agc atg ttg gtc atc ctt ctc aac tgc gtg Pro Trp Phe Glu Arg Ile Ser Met Leu Val Ile Leu Leu Asn Cys Val	288
	85 90 95	
60	acc ctg ggc atg ttc ccg cca tgc gag gac atc gcc tgt gac tcc cag Thr Leu Gly Met Phe Arg Pro Cys Glu Asp Ile Ala Cys Asp Ser Gln	336
	100 105 110	
	cgc tgc ccg atc ctg cag gcc ttt gat gac ttc atc ttt gcc ttc ttt Arg Cys Arg Ile Leu Gln Ala Phe Asp Asp Phe Ile Phe Ala Phe Phe	384
	115 120 125	
	gcc gtg gag atg gtg gtg aag atg gtg gcc ttg ggc atc ttt ggg aaa Ala Val Glu Met Val Val Lys Met Val Ala Leu Gly Ile Phe Gly Lys	432

	130	135	140	
5	aag tgt tac ctg gga gac act tgg aac cgg ctt gac ttt ttc atc gtc Lys Cys Tyr Leu Gly Asp Thr Trp Asn Arg Leu Asp Phe Phe Ile Val			480
	145	150	155	160
	atc gca ggg atg ctg gag tac tcg ctg gac ctg cag aac gtc agc ttc Ile Ala Gly Met Leu Glu Tyr Ser Leu Asp Leu Gln Asn Val Ser Phe			528
10	165	170	175	
	tca gct gtc agg aca gtc cgt gtg ctg cga ccg ctc agg gcc att aac Ser Ala Val Arg Thr Val Arg Val Leu Arg Pro Leu Arg Ala Ile Asn			576
	180	185	190	
15	cgg gtg ccc agc atg cgc atc ctt gtc acg ttg ctg ctg gat acg ctg Arg Val Pro Ser Met Arg Ile Leu Val Thr Leu Leu Leu Asp Thr Leu			624
	195	200	205	
20	ccc atg ctg ggc aac gtc ctg ctg ctc tgc ttc gtc ttc ttc atc Pro Met Leu Gly Asn Val Leu Leu Leu Cys Phe Phe Val Phe Phe Ile			672
	210	215	220	
25	ttc ggc atc gtc ggc gtc cag ctg tgg gca ggg ctg ctt cgg aac cga Phe Gly Ile Val Gly Val Gln Leu Trp Ala Gly Leu Leu Arg Asn Arg			720
	225	230	235	240
	tgc ttc cta cct gag aat ttc agc ctc ccc ctg agc gtg gac ctg gag Cys Phe Leu Pro Glu Asn Phe Ser Leu Pro Leu Ser Val Asp Leu Glu			768
30	245	250	255	
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	260	265	270	
35	cag cca cgc gag aac ggc atg cgg tcc tgc aga agc gtg ccc acg ctg Gln Pro Arg Glu Asn Gly Met Arg Ser Cys Arg Ser Val Pro Thr Leu			864
	275	280	285	
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	290	295	300	
45	tac aac agc tcc agc aac acc acc tgg gtc aac tgg aac cag tac tac Tyr Asn Ser Ser Asn Thr Thr Cys Val Asn Trp Asn Gln Tyr Tyr			960
	305	310	315	320
	acc aac tgc tca gcg ggg gag cac aac ccc ttc aag ggc gcc atc aac Thr Asn Cys Ser Ala Gly Glu His Asn Pro Phe Lys Gly Ala Ile Asn			1008
50	325	330	335	
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	340	345	350	
55	ctg gag ggc tgg gtc gac atc atg tac ttt gtg atg gat gct cat tcc Leu Glu Gly Trp Val Asp Ile Met Tyr Phe Val Met Asp Ala His Ser			1104
	355	360	365	
60	ttc tac aat ttc atc tac ttc atc ctc ctc atc atc gtg ggc tcc ttc Phe Tyr Asn Phe Ile Tyr Phe Ile Leu Leu Ile Ile Val Gly Ser Phe			1152
	370	375	380	
	ttc atg atc aac ctg tgc ctg gtg att gcc acg cag ttc tca gag Phe Met Ile Asn Leu Cys Leu Val Val Ile Ala Thr Gln Phe Ser Glu			1200

385	390	395	400		
acc aag cag cg ₃ gaa agc cag ctg atg cg ₂ gag cag cgt gt ₂ cg ₂ ttc Thr Lys Gln Arg Glu Ser Gln Leu Met Arg Glu Gln Arg Val Arg Phe					
5	405	410	415	1248	
ctg tcc aac gcc agc acc ctg gct agc ttc tct gag ccc ggc agc tgc Leu Ser Asn Ala Ser Thr Leu Ala Ser Phe Ser Glu Pro Gly Ser Cys					
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tat gag gag ctg ctc aag tac ctg gt ₂ tac atc ctt cgt aag gca gcc Tyr Glu Glu Leu Leu Lys Tyr Leu Val Tyr Ile Leu Arg Lys Ala Ala					
	435	440	445	1344	
15	cg ₂ agg ctg gct cag gtc tct cg ₂ gca gca ggt gt ₂ cg ₂ gtt ggg ctg Arg Arg Leu Ala Gln Val Ser Arg Ala Ala Gly Val Arg Val Gly Leu				1392
	450	455	460		
20	ctc agc agc cca gca ccc ctc ggg ggc cag gag acc cag ccc agc agc Leu Ser Ser Pro Ala Pro Leu Gly Gly Gln Glu Thr Gln Pro Ser Ser				1440
	465	470	475	480	
25	agc tgc tct cg ₂ tcc cac cg ₂ cta tcc gtc cac cac ctg gt ₂ cac Ser Cys Ser Arg Ser His Arg Arg Leu Ser Val His His Leu Val His				1488
	485	490	495		
30	cac cac cac cat cac cac tac cac ctg ggc aat ggg acg ctc His His His His His His Tyr His Leu Gly Asn Gly Thr Leu				1536
	500	505	510		
agg gcc ccc cg ₂ gcc agc cc ₂ gag atc cag gac agg gat gcc aat ggg Arg Ala Pro Arg Ala Ser Pro Glu Ile Gln Asp Arg Asp Ala Asn Gly					1584
	515	520	525		
35	tcc cg ₂ cgg ctc atg ctg cca cca ccc tcg acg cct gcc ctc tcc ggg Ser Arg Arg Leu Met Leu Pro Pro Pro Ser Thr Pro Ala Leu Ser Gly				1632
	530	535	540		
40	gcc ccc cct ggt ggc gca gag tct gt ₂ cac agc ttc tac cat gcc gac Ala Pro Pro Gly Gly Ala Glu Ser Val His Ser Phe Tyr His Ala Asp				1680
	545	550	555	560	
45	tgc cac tta gag cca gtc cg ₂ tgc cag g ₂ ccc cct ccc agg tcc cca Cys His Leu Glu Pro Val Arg Cys Gln Ala Pro Pro Pro Arg Ser Pro				1728
	565	570	575		
50	tct gag gca tcc ggc agg act gt ₂ ggc agc ggg aag gt ₂ tat ccc acc Ser Glu Ala Ser Gly Arg Thr Val Gly Ser Gly Lys Val Tyr Pro Thr				1776
	580	585	590		
gt ₂ cac acc agc cct cca cc ₂ gag acg ctg aag gag aag gca cta gta Val His Thr Ser Pro Pro Pro Glu Thr Leu Lys Glu Lys Ala Leu Val					1824
	595	600	605		
55	gag gt ₂ gct gcc agc tct ggg ccc cca acc ctc acc agc ctc aac atc Glu Val Ala Ala Ser Ser Gly Pro Pro Thr Leu Thr Ser Leu Asn Ile				1872
	610	615	620		
60	cca ccc ggg ccc tac agc tcc atg cac aag ctg ctg gag aca cag agt Pro Pro Gly Pro Tyr Ser Ser Met His Lys Leu Leu Glu Thr Gln Ser				1920
	625	630	635	640	
aca ggt gcc tgc caa agc tct tgc aag atc tcc agc cct tgc ttg aaa Thr Gly Ala Cys Gln Ser Ser Cys Lys Ile Ser Ser Pro Cys Leu Lys					1968

	645	650	655	
5	gca gac agt gga gcc tgt ggt cca gac agc tgc ccc tac tgt gcc cgg Aia Asp Ser Gly Ala Cys Gly Pro Asp Ser Cys Pro Tyr Cys Ala Arg 660	665	670	2016
10	gcc ggg gca ggg gag gtg gag ctc gcc gac cgt gaa atg cct gac tca Ala Gly Ala Gly Glu Val Glu Leu Ala Asp Arg Glu Met Pro Asp Ser 675	680	685	2064
15	gac agc gag gca gtt tat gag ttc aca cag gat gcc cag cac agc gac Asp Ser Glu Ala Val Tyr Glu Phe Thr Gln Asp Ala Gln His Ser Asp 690	695	700	2112
20	ctc cgg gac ccc cac agc cg ^g caa cg ^g agc ctg gg ^c cca gat gca Leu Arg Asp Pro His Ser Arg Arg Gln Arg Ser Leu Gly Pro Asp Ala 705	710	715	2160
25	gag ccc agc tct gtg ctg gcc ttc tgg agg cta atc tgt gac acc ttc Glu Pro Ser Ser Val Leu Ala Phe Trp Arg Leu Ile Cys Asp Thr Phe 725	730	735	2208
30	cga aag att gtg gac agc aag tac ttt ggc cg ^g gga atc atg atc gcc Arg Lys Ile Val Asp Ser Lys Tyr Phe Gly Arg Gly Ile Met Ile Ala 740	745	750	2256
35	atc ctg gtc aac aca ctc agc atg ggc atc gaa tac cac gag cag ccc Ile Leu Val Asn Thr Leu Ser Met Gly Ile Glu Tyr His Glu Gln Pro 755	760	765	2304
40	gag gag ctt acc aac gcc cta gaa atc agc aac atc gtc ttc acc agc Glu Glu Leu Thr Asn Ala Leu Glu Ile Ser Asn Ile Val Phe Thr Ser 770	775	780	2352
45	ctc ttt gcc ctg gag atg ctg ctg aag ctg ctt gtg tat ggt ccc ttt Leu Phe Ala Leu Glu Met Leu Leu Lys Leu Val Tyr Gly Pro Phe 785	790	795	2400
50	ggc tac atc aag aat ccc tac aac atc ttc gat ggt gtc att gtg gtc Gly Tyr Ile Lys Asn Pro Tyr Asn Ile Phe Asp Gly Val Ile Val Val 805	810	815	2448
55	atc agc gtg tgg gag atc gtg ggc cag cag ggg ggc ggc ctg tcg gtg Ile Ser Val Trp Glu Ile Val Gly Gln Gln Gly Gly Leu Ser Val 820	825	830	2496
60	ctg cgg acc ttc cgc ctg atg cgt gtg ctg aag ctg gtg cgc ttc ctg Leu Arg Thr Phe Arg Leu Met Arg Val Leu Lys Leu Val Arg Phe Leu 835	840	845	2544
65	ccg gcg ctg cag cg ^g cag ctg gtg ctc atg aag acc atg gac aac Pro Ala Leu Gln Arg Gln Leu Val Val Leu Met Lys Thr Met Asp Asn 850	855	860	2592
70	gtg gcc acc ttc tgc atg ctg ctt atg ctc ttc atc ttc atc ttc agc Val Ala Thr Phe Cys Met Leu Leu Met Leu Phe Ile Phe Ile Phe Ser 865	870	875	2640
75	atc ctg ggc atg cat ctc ttc ggc tgc aag ttt gcc tct gag cg ^g gat Ile Leu Gly Met His Leu Phe Gly Cys Lys Phe Ala Ser Glu Arg Asp 885	890	895	2688
80	ggg gac acc ctg cca gac cg ^g aag aat ttt gac tcc ttg ctc tgg gcc Gly Asp Thr Leu Pro Asp Arg Lys Asn Phe Asp Ser Leu Leu Trp Ala 905			2736

	900	905	910	
5	atc gtc act gtc ttt cag atc ctg acc cag gag gac tgg aac aaa gtc Ile Val Thr Val Phe Gln Ile Leu Thr Gln Glu Asp Trp Asn Lys Val 915 920 925			2784
10	ctc tac aat ggt atg gcc tcc acg tcg tcc tgg gcg gcc ctt tat ttc Leu Tyr Asn Gly Met Ala Ser Thr Ser Trp Ala Ala Leu Tyr Phe 930 935 940			2832
15	att gcc ctc atg acc ttc ggc aac tac gtg ctc ttc aat ttg ctg gtc Ile Ala Leu Met Thr Phe Gly Asn Tyr Val Leu Phe Asn Leu Leu Val 945 950 955 960			2880
20	gcc att ctg gtg gag ggc ttc cag gcg gag gga gat gcc aac aag tcc Ala Ile Leu Val Glu Gly Phe Gln Ala Glu Gly Asp Ala Asn Lys Ser 965 970 975			2928
25	gaa tca gag ccc gat ttc ttc tca ccc agc ctg gat ggt gat ggg gac Glu Ser Glu Pro Asp Phe Ser Pro Ser Leu Asp Gly Asp Gly Asp 980 985 990			2976
30	agg aag aag tgc ttg gcc ttg gtg tcc ctg gga gag cac ccg gag ctg Arg Lys Lys Cys Leu Ala Leu Val Ser Leu Gly Glu His Pro Glu Leu 995 1000 1005			3024
35	cgg aag agc ctg ctg ccg cct ctc atc atc cac acg gcc gcc aca ccc Arg Lys Ser Leu Leu Pro Pro Leu Ile Ile His Thr Ala Ala Thr Pro 1010 1015 1020			3072
40	atg tcg ctg ccc aag agc acc agc acg ggc ctg ggc gag gcg ctg ggc Met Ser Leu Pro Lys Ser Thr Ser Thr Gly Leu Gly Glu Ala Leu Gly 1025 1030 1035 1040			3120
45	cct gcg tcg cgc cgc acc agc agc ggg tcg gca gag cct ggg gcg Pro Ala Ser Arg Arg Thr Ser Ser Ser Gly Ser Ala Glu Pro Gly Ala 1045 1050 1055			3168
50	gcc cac gag atg aag tca ccg ccc agc gcc cgc agc tct ccg cac agc Ala His Glu Met Lys Ser Pro Pro Ser Ala Arg Ser Ser Pro His Ser 1060 1065 1070			3216
55	ccc tgg agc gct gca agc agc tgg acc agc agg cgc tcc agc cgg aac Pro Trp Ser Ala Ala Ser Ser Trp Thr Ser Arg Arg Ser Ser Arg Asn 1075 1080 1085			3264
60	agc ctc ggc cgt gca ccc agc ctg aag cgg aga agc cca agt gga gag Ser Leu Gly Arg Ala Pro Ser Leu Lys Arg Arg Ser Pro Ser Gly Glu 1090 1095 1100			3312
65	cgg cgg tcc ctg ttg tcg gga gaa ggc cag gag agc cag gat gaa gag Arg Arg Ser Leu Leu Ser Gly Glu Gly Gln Glu Ser Gln Asp Glu Glu 1105 1110 1115 1120			3360
70	gag agc tca gaa gag gag cgg gcc agc cct gcg ggc agt gac cat cgc Glu Ser Ser Glu Glu Arg Ala Ser Pro Ala Gly Ser Asp His Arg 1125 1130 1135			3408
75	cac agg ggg tcc ctg gag cgg gag gcc aag agt tcc ttt gac ctg cca His Arg Gly Ser Leu Glu Arg Glu Ala Lys Ser Ser Phe Asp Leu Pro 1140 1145 1150			3456
80	gac aca ctg cag gtg cca ggg ctg cat cgc act gcc agt ggc cga ggg Asp Thr Leu Gln Val Pro Gly Leu His Arg Thr Ala Ser Gly Arg Gly			3504

	1155	1160	1165	
5	tct gct tct gag cac cag gac tgc aat ggc aag tcg gct tca ggg cgc Ser Ala Ser Glu His Gln Asp Cys Asn Gly Lys Ser Ala Ser Gly Arg 1170 1175 1180			3552
10	ctg gcc cggttgc ctttgc ctttgc gat gac ccc cca ctg gat ggg gat gac Leu Ala Arg Ala Leu Arg Pro Asp Asp Pro Pro Leu Asp Gly Asp Asp 1185 1190 1195 1200			3600
15	gcc gat gac gag ggc aac ctg agc aaa ggg gaa cgg gtc cgc gcg tgg Ala Asp Asp Glu Gly Asn Leu Ser Lys Gly Glu Arg Val Arg Ala Trp 1205 1210 1215			3648
20	atc cga gcc cga ctc cct gcc tgc tgc ctc gag cga gac tcc tgg tca Ile Arg Ala Arg Leu Pro Ala Cys Cys Leu Glu Arg Asp Ser Trp Ser 1220 1225 1230			3696
25	gcc tac atc ttc cct cag tcc agg ttc cgc ctc ctg tgt cac cgg Ala Tyr Ile Phe Pro Pro Gln Ser Arg Phe Arg Leu Leu Cys His Arg 1235 1240 1245			3744
30	atc atc acc cac aag atg ttc gac cac gtg gtc ctt gtc atc atc ttc Ile Ile Thr His Lys Met Phe Asp His Val Val Leu Val Ile Ile Phe 1250 1255 1260			3792
35	ctt aac tgc atc acc atc gcc atg gag cgc ccc aaa att gac ccc cac Leu Asn Cys Ile Thr Ile Ala Met Glu Arg Pro Lys Ile Asp Pro His 1265 1270 1275 1280			3840
40	agc gct gaa cgc atc ttc ctg acc ctc tcc aat tac atc ttc acc gca Ser Ala Glu Arg Ile Phe Leu Thr Leu Ser Asn Tyr Ile Phe Thr Ala 1285 1290 1295			3888
45	gtc ttt ctg gct gaa atg aca gtg aag gtg gtg gca ctg ggc tgg tgc Val Phe Leu Ala Glu Met Thr Val Lys Val Val Ala Leu Gly Trp Cys 1300 1305 1310			3936
50	ttc ggg gag cag gcg tac ctg cgg agc agt tgg aac gtg ctg gac ggg Phe Gly Glu Gln Ala Tyr Leu Arg Ser Ser Trp Asn Val Leu Asp Gly 1315 1320 1325			3984
55	ctg ttg gtg ctc atc tcc gtc atc gac att ctg gtg tcc atg gtc tct Leu Leu Val Leu Ile Ser Val Ile Asp Ile Leu Val Ser Met Val Ser 1330 1335 1340			4032
60	gac agc ggc acc aag atc ctg ggc atg ctg agg gtg ctg cgg ctg ctg Asp Ser Gly Thr Lys Ile Leu Gly Met Leu Arg Val Leu Arg Leu Leu 1345 1350 1355 1360			4080
65	cgg acc ctg cgc ccg ctc agg gtg atc agc cgg gcg cag ggg ctg aag Arg Thr Leu Arg Pro Leu Arg Val Ile Ser Arg Ala Gln Gly Leu Lys 1365 1370 1375			4128
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75	gta gtc atc tgc tgt gcc ttc ttc atc att ttc ggc atc ttg ggg gtg Val Val Ile Cys Cys Ala Phe Phe Ile Ile Phe Gly Ile Leu Gly Val 1395 1400 1405			4224
80	cag ctc ttc aaa ggg aag ttt ttc gtg tgc cag ggc gag gat acc agg Gln Leu Phe Lys Gly Lys Phe Phe Val Cys Gln Gly Glu Asp Thr Arg			4272

	1410	1415	1420	
5	aac atc acc aat aaa tcg gac tgt gcc gag gcc agt tac cgg tgg gtc Asn Ile Thr Asn Lys Ser Asp Cys Ala Glu Ala Ser Tyr Arg Trp Val 1425 1430 1435 1440			4320
10	cgg cac aag tac aac ttt gac aac ctt ggc cag gcc ctg atg tcc ctg Arg His Lys Tyr Asn Phe Asp Asn Leu Gly Gin Ala Leu Met Ser Leu 1445 1450 1455			4368
15	ttc gtt ttg gcc tcc aag gat ggt tgg gtg gac atc atg tac gat ggg Phe Val Leu Ala Ser Lys Asp Gly Trp Val Asp Ile Met Tyr Asp Gly 1460 1465 1470			4416
20	ctg gat gct gtg ggc gtg gac cag ccc atc atg aac cac aac ccc Leu Asp Ala Val Gly Val Asp Gln Gln Pro Ile Met Asn His Asn Pro 1475 1480 1485			4464
25	tgg atg ctg ctg tac ttc atc tcg ttc ctg ctc att gtg gcc ttc ttt Trp Met Leu Leu Tyr Phe Ile Ser Phe Leu Leu Ile Val Ala Phe Phe 1490 1495 1500			4512
30	gtc ctg aac atg ttt gtg ggt gtg gtg gtg gag aac ttc cac aag tgt Val Leu Asn Met Phe Val Gly Val Val Val Glu Asn Phe His Lys Cys 1505 1510 1515 1520			4560
35	cgg cag cac cag gag gaa gag gag gcc cgg cgg cgg gag aag cgc Arg Gln His Gln Glu Glu Glu Ala Arg Arg Arg Glu Glu Lys Arg 1525 1530 1535			4608
40	cta cga aga ctg gag aaa aag aga agg aat cta atg ctg gac gat gta Leu Arg Arg Leu Glu Lys Lys Arg Arg Asn Leu Met Leu Asp Asp Val 1540 1545 1550			4656
45	att gct tcc ggc agc tca gcc agc gct gcg tca gaa gcc cag tgc aaa Ile Ala Ser Gly Ser Ser Ala Ser Ala Ala Ser Glu Ala Gln Cys Lys 1555 1560 1565			4704
50	cct tac tac tcc gac tac tcc cgc ttc cgg ctc ctc gtc cac cac ttg Pro Tyr Tyr Ser Asp Tyr Ser Arg Phe Arg Leu Leu Val His His Leu 1570 1575 1580			4752
55	tgc acc agc cac tac ctg gac ctc ttc atc aca ggt gtc atc ggg ctg Cys Thr Ser His Tyr Leu Asp Leu Phe Ile Thr Gly Val Ile Gly Leu 1585 1590 1595 1600			4800
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65	gat gag gct ctg aag atc tgc aac tac atc ttc act gtc atc ttt gtc Asp Glu Ala Leu Lys Ile Cys Asn Tyr Ile Phe Thr Val Ile Phe Val 1620 1625 1630			4896
70	ttg gag tca gtt ttc aaa ctt gtg gcc ttt ggt ttc cgt cgg ttc ttc Leu Glu Ser Val Phe Lys Leu Val Ala Phe Gly Phe Arg Arg Phe Phe 1635 1640 1645			4944
75	cag gac agg tgg aac cag ctg gac ctg gcc att gtg ctg ctg tcc atc Gln Asp Arg Trp Asn Gln Leu Asp Leu Ala Ile Val Leu Leu Ser Ile 1650 1655 1660			4992
80	atg ggc atc acg ctg gag gaa atc gag gtc aac gcc tcg ctg ccc atc Met Gly Ile Thr Leu Glu Glu Ile Glu Val Asn Ala Ser Leu Pro Ile			5040

	1665	1670	1675	1680	
5	aac ccc acc atc atc cgc atc atg agg gtg ctg cgc att gcc cga gtg Asn Pro Thr Ile Ile Arg Ile Met Arg Val Leu Arg Ile Ala Arg Val				5088
	1685		1690	1695	
	ctg aag ctg ctg aag atg gct gtg ggc atg cgg gcg ctg ctg gac acg Leu Lys Leu Leu Lys Met Ala Val Gly Met Arg Ala Leu Leu Asp Thr				5136
10	1700	1705		1710	
	gtg atg cag gcc ctg ccc cag gtg ggg aac ctg gga ctt ctc ttc atg Val Met Gln Ala Leu Pro Gln Val Gly Asn Leu Gly Leu Leu Phe Met				5184
	1715	1720	1725		
15	ttg ttg ttt ttc atc ttt gca gct ctg ggc gtg gag ctc ttt gga gac Leu Leu Phe Phe Ile Phe Ala Ala Leu Gly Val Glu Leu Phe Gly Asp				5232
	1730	1735	1740		
20	ctg gag tgt gac gag aca cac ccc tgt gag ggc ctg ggc cgt cat gcc Leu Glu Cys Asp Glu Thr His Pro Cys Glu Gly Leu Gly Arg His Ala				5280
	1745	1750	1755	1760	
25	acc ttt cgg aac ttt ggc atg gcc ttc cta acc ctc ttc cga gtc tcc Thr Phe Arg Asn Phe Gly Met Ala Phe Leu Thr Leu Phe Arg Val Ser				5328
	1765	1770	1775		
	aca ggt gac aat tgg aat ggc att atg aag gac acc ctc cgg gac tgt Thr Gly Asp Asn Trp Asn Gly Ile Met Lys Asp Thr Leu Arg Asp Cys				5376
30	1780	1785	1790		
	gac cag gag tcc acc tgc tac aac acg gtc atc tcg cct atc tac ttt Asp Gln Glu Ser Thr Cys Tyr Asn Thr Val Ile Ser Pro Ile Tyr Phe				5424
	1795	1800	1805		
35	gtg tcc ttc gtg ctg acg gcc cag ttc gtg cta gtc aac gtg gtg atc Val Ser Phe Val Leu Thr Ala Gln Phe Val Leu Val Asn Val Val Ile				5472
	1810	1815	1820		
40	gcc gtg ctg atg aag cac ctg gag gag agc aac aag gag gcc aag gag Ala Val Leu Met Lys His Leu Glu Glu Ser Asn Lys Glu Ala Lys Glu				5520
	1825	1830	1835	1840	
45	gag gcc gag cta gag gct gag ctg gag ctg gag atg aag acc ctc agc Glu Ala Glu Leu Ala Glu Leu Glu Leu Glu Met Lys Thr Leu Ser				5568
	1845	1850	1855		
	ccc cag ccc cac tcg cca ctg ggc agc ccc ttc ctc tgg cct ggg gtc Pro Gln Pro His Ser Pro Leu Gly Ser Pro Phe Leu Trp Pro Gly Val				5616
50	1860	1865	1870		
	gag ggc ccc gac agc ccc gac agc ccc aag cct ggg gct ctg cac cca Glu Gly Pro Asp Ser Pro Asp Ser Pro Lys Pro Gly Ala Leu His Pro				5664
	1875	1880	1885		
55	gcg gcc cac gcg aga tca gcc tcc cac ttt tcc ctg gag cac ccc acg Ala Ala His Ala Arg Ser Ala Ser His Phe Ser Leu Glu His Pro Thr				5712
	1890	1895	1900		
60	atg cag ccc cac ccc acg gag ctg cca gga cca gac tta ctg act gtg Met Gln Pro His Pro Thr Glu Leu Pro Gly Pro Asp Leu Leu Thr Val				5760
	1905	1910	1915	1920	
	cgg aag tct ggg gtc agc cga acg cac tct ctg ccc aat gac agc tac Arg Lys Ser Gly Val Ser Arg Thr His Ser Leu Pro Asn Asp Ser Tyr				5808

	1925	1930	1935	
5	atg tgt cgg cat ggg agc act gcc gag ggg ccc ctg gga cac agg ggc Met Cys Arg His Gly Ser Thr Ala Glu Gly Pro Leu Gly His Arg Gly 1940 1945 1950			5856
10	tgg ggg ctc ccc aaa gct caq tca ggc tcc gtc ttg tcc gtt cac tcc Trp Gly Leu Pro Lys Ala Gln Ser Gly Ser Val Leu Ser Val His Ser 1955 1960 1965			5904
15	cag cca gca gat acc agc tac atc ctg cag ctt ccc aaa gat gca cct Gln Pro Ala Asp Thr Ser Tyr Ile Leu Gln Leu Pro Lys Asp Ala Pro 1970 1975 1980			5952
20	cat ctg ctc cag ccc cac agc gcc cca acc tgg ggc acc atc ccc aaa His Leu Leu Gln Pro His Ser Ala Pro Thr Trp Gly Thr Ile Pro Lys 1985 1990 1995 2000			6000
25	ctg ccc cca cca gga cgc tcc cct ttg gct cag agg cca ctc agg cgc Leu Pro Pro Pro Gly Arg Ser Pro Leu Ala Gln Arg Pro Leu Arg Arg 2005 2010 2015			6048
30	cag gca gca ata agg act gac tcc ttg gac gtt cag ggt ctg ggc agc Gln Ala Ala Ile Arg Thr Asp Ser Leu Asp Val Gln Gly Leu Gly Ser 2020 2025 2030			6096
35	cgg gaa gac ctg ctg gca gag gtg agt ggg ccc tcc ccg ccc ctg gcc Arg Glu Asp Leu Leu Ala Glu Val Ser Gly Pro Ser Pro Pro Leu Ala 2035 2040 2045			6144
40	cgg gcc tac tct ttc ttg ggc cag tca agt acc cag gca cag cag cac Arg Ala Tyr Ser Phe Trp Gly Gln Ser Ser Thr Gln Ala Gln Gln His 2050 2055 2060			6192
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50	tgc cca ggc cca gaa ccc aac ttg ggc aag ggc cct cca gag acc aga Cys Pro Gly Pro Glu Pro Asn Trp Gly Lys Gly Pro Pro Glu Thr Arg 2085 2090 2095			6288
55	agc agc tta gag ttg gac acg gag ctg agc ttg att tca gga gac ctc Ser Ser Leu Glu Leu Asp Thr Glu Leu Ser Trp Ile Ser Gly Asp Leu 2100 2105 2110			6336
60	ctg ccc cct ggc ggc cag gag gag ccc cca tcc cca cggt gac ctg aag Leu Pro Pro Gly Gly Gln Glu Glu Pro Pro Ser Pro Arg Asp Leu Lys 2115 2120 2125			6384
65	aag tgc tac agc gtg gag gcc cag agc tgc cag cgc cgg cct acg tcc Lys Cys Tyr Ser Val Glu Ala Gln Ser Cys Gln Arg Arg Pro Thr Ser 2130 2135 2140			6432
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80	cag cct ctt ggg ggg cct ggg agc cgg ccc aag aaa aaa ctc agc ccg Gln Pro Leu Gly Gly Pro Gly Ser Arg Pro Lys Lys Lys Leu Ser Pro			6576

	2180	2185	2190	
5	cct agt atc acc ata gas ccc ccc gag agc caa ggt cct cgg acc ccg Pro Ser Ile Thr Ile Asp Pro Pro Glu Ser Gin Gly Pro Arg Thr Pro 2195 2200 2205			6624
10	ccc agc cct ggt atc tgc ctc cgg agg agg gct ccc tcc agc gac tcc Pro Ser Pro Gly Ile Cys Leu Arg Arg Ala Pro Ser Ser Asp Ser 2210 2215 2220			6672
15	aag gat ccc ttg gcc tct ggc ccc cct gac agc atg gct gcc tcc ccc Lys Asp Pro Leu Ala Ser Gly Pro Pro Asp Ser Met Ala Ala Ser Pro 2225 2230 2235 2240			6720
20	tcc cca aag aaa gat gtg ctg agt ctc tcc ggt tta tcc tct gac cca Ser Pro Lys Lys Asp Val Leu Ser Leu Ser Gly Leu Ser Ser Asp Pro 2245 2250 2255			6769
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50	ggg ccg ggg tca gca gaa aag gac ccg ggc agc gcg gac tcc gag gcg Gly Pro Gly Ser Ala Glu Lys Asp Pro Gly Ser Ala Asp Ser Glu Ala 35 40 45			144
55	gag ggg ctg ccg tac ccg gcg ctg gcc ccg gtg gtt ttc ttc tac ttg Glu Gly Leu Pro Tyr Pro Ala Leu Ala Pro Val Val Phe Phe Tyr Leu 50 55 60			192
60	agc cag gac agc cgc ccg cgg agc tgg tgt ctc cgc acg gtc tgt aac Ser Gln Asp Ser Arg Pro Arg Ser Trp Cys Leu Arg Thr Val Cys Asn 65 70 75 80			240
65	ccc tgg ttt gag cgc atc agc atg ttg gtc atc ctt ctc aac tgc gtg Pro Trp Phe Glu Arg Ile Ser Met Leu Val Ile Leu Leu Asn Cys Val 85 90 95			288
70	acc ctg ggc atg ttc cgg cca tgc gag gac atc gcc tgt gac tcc cag Thr Leu Gly Met Phe Arg Pro Cys Glu Asp Ile Ala Cys Asp Ser Gln 100 105 110			336
75	cgc tgc cgg atc ctg cag gcc ttt gat gac ttc atc ttt gcc ttc ttt Arg Cys Arg Ile Leu Gin Ala Phe Asp Asp Phe Ile Phe Ala Phe Phe 115 120 125			384

5	gcc gtg gag atg gtg gtc aag atg gtg gcc ttg ggc atc ttt ggg aaa Ala Val Glu Met Val Val Lys Met Val Ala Leu Gly Ile Phe Gly Lys 130 135 140	432
10	aag tgt tac ctg gga gac act tgg aac cgg ctt gac ttt ttc atc gtc Lys Cys Tyr Leu Gly Asp Thr Trp Asn Arg Leu Asp Phe Phe Ile Val 145 150 155 160	480
15	atc gca ggg atg ctg gag tac tcg ctg gac ctg cag aac gtc agc ttc Ile Ala Glu Met Leu Glu Tyr Ser Leu Asp Leu Gln Asn Val Ser Phe 165 170 175	528
20	tca gct gtc agg aca gtc cgt gtg ctg cga ccg ctc agg gcc att aac Ser Ala Val Arg Thr Val Arg Val Leu Arg Pro Leu Arg Ala Ile Asn 180 185 190	576
25	cgg gtg ccc agc atg cgc atc ctt gtc acg ttg ctg ctg gat acg ctg Arg Val Pro Ser Met Arg Ile Leu Val Thr Leu Leu Leu Asp Thr Leu 195 200 205	624
30	ccc atg ctg ggc aac gtc ctg ctg ctc tgc ttc ttc gtc ttc ttc atc Pro Met Leu Gly Asn Val Leu Leu Leu Cys Phe Phe Val Phe Phe Ile 210 215 220	672
35	ttc ggc atc gtc ggc gtc cag ctg tgg gca ggg ctg ctt cgg aac cga Phe Gly Ile Val Gly Val Gln Leu Trp Ala Gly Leu Leu Arg Asn Arg 225 230 235 240	720
40	tgc ttc cta cct gag aat ttc agc ctc ccc ctg agc gtg gac ctg gag Cys Phe Leu Pro Glu Asn Phe Ser Leu Pro Leu Ser Val Asp Leu Glu 245 250 255	768
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50	cag cca cgc gag aac ggc atg cgg tcc tgc aga agc gtg ccc acg ctg Gln Pro Arg Glu Asn Gly Met Arg Ser Cys Arg Ser Val Pro Thr Leu 275 280 285	864
55	cgc ggg gac ggg ggc ggt ggc cca cct tgc ggt ctg gac tat gag gcc Arg Gly Asp Gly Gly Pro Pro Cys Gly Leu Asp Tyr Glu Ala 290 295 300	912
60	tac aac agc tcc agc aac acc acc ttt gtc aac tgg aac cag tac tac Tyr Asn Ser Ser Asn Thr Thr Cys Val Asn Trp Asn Gln Tyr Tyr 305 310 315 320	960
65	acc aac tgc tca gcg ggg gag cac aac ccc ttc aag ggc gcc atc aac Thr Asn Cys Ser Ala Gly Glu His Asn Pro Phe Lys Gly Ala Ile Asn 325 330 335	1008
70	ttt gac aac att ggc tat gcc tgg atc gcc atc ttc cag gtc atc acg Phe Asp Asn Ile Gly Tyr Ala Trp Ile Ala Ile Phe Gln Val Ile Thr 340 345 350	1056
75	ctg gag ggc tgg gtc gac atc atg tac ttt gtg atg gat gct cat tcc Leu Glu Gly Trp Val Asp Ile Met Tyr Phe Val Met Asp Ala His Ser 355 360 365	1104
80	ttc tac aat ttc atc tac ttc atc ctc ctc atc atc gtg ggc tcc ttc Phe Tyr Asn Phe Ile Tyr Phe Ile Leu Leu Ile Ile Val Gly Ser Phe 370 375 380	1152

	ttc atg atc aac ctg tgc ctg gtg gtc att gcc acg cag ttc tca gag	1200		
	Phe Met Ile Asn Leu Cys Leu Val Val Ile Ala Thr Gin Phe Ser Glu			
385	390	395	400	
5	acc aag cag cgg gaa agc cag ctg atg cgg gag cag cgt gtg cgg ttc	1248		
	Thr Lys Gln Arg Glu Ser Gin Leu Met Arg Glu Gin Arg Val Arg Phe			
	405	410	415	
10	ctg tcc aac gcc agc acc ctg gct agc ttc tct gag ccc ggc agc tgc	1296		
	Leu Ser Asn Ala Ser Thr Leu Ala Ser Phe Ser Glu Pro Gly Ser Cys			
	420	425	430	
15	tat gag gag ctg ctc aag tac ctg gtg tac atc ctt cgt aag gca gcc	1344		
	Tyr Glu Glu Leu Leu Lys Tyr Leu Val Tyr Ile Leu Arg Lys Ala Ala			
	435	440	445	
20	cgc agg ctg gct cag gtc tct cgg gca gca ggt gtg cgg gtt ggg ctg	1392		
	Arg Arg Leu Ala Gln Val Ser Arg Ala Ala Gly Val Arg Val Gly Leu			
	450	455	460	
	ctc agc agc cca gca ccc ctc ggg ggc cag gag acc cag ccc agc agc	1440		
	Leu Ser Ser Pro Ala Pro Leu Gly Gly Gln Glu Thr Gln Pro Ser Ser			
	465	470	475	480
25	agc tgc tct cgc tcc cac cgc cgc cta tcc gtc cac cac ctg gtg cac	1488		
	Ser Cys Ser Arg Ser His Arg Arg Leu Ser Val His His Leu Val His			
	485	490	495	
30	cac cac cac cat cac cac tac cac ctg ggc aat ggg acg ctc	1536		
	His His His His His His Tyr His Leu Gly Asn Gly Thr Leu			
	500	505	510	
35	agg gcc ccc cgg gcc agc ccg gag atc cag gac agg gat gcc aat ggg	1584		
	Arg Ala Pro Arg Ala Ser Pro Glu Ile Gln Asp Arg Asp Ala Asn Gly			
	515	520	525	
40	tcc cgc cgg ctc atg ctg cca cca ccc tcg acg cct gcc ctc tcc ggg	1632		
	Ser Arg Arg Leu Met Leu Pro Pro Ser Thr Pro Ala Leu Ser Gly			
	530	535	540	
	gcc ccc cct ggt ggc gca gag tct gtg cac acg ttc tac cat gcc gac	1680		
	Ala Pro Pro Gly Gly Ala Glu Ser Val His Ser Phe Tyr His Ala Asp			
	545	550	555	560
45	tgc cac tta gag cca gtc cgc tgc cag gcg ccc cct ccc agg tcc cca	1728		
	Cys His Leu Glu Pro Val Arg Cys Gln Ala Pro Pro Pro Arg Ser Pro			
	565	570	575	
50	tct gag gca tcc ggc agg act gtg ggc agc ggg aag gtg tat ccc acc	1776		
	Ser Glu Ala Ser Gly Arg Thr Val Gly Ser Gly Lys Val Tyr Pro Thr			
	580	585	590	
55	gtg cac acc agc cct cca ccg gag acg ctg aag gag aag gca cta gta	1824		
	Val His Thr Ser Pro Pro Glu Thr Leu Lys Glu Lys Ala Leu Val			
	595	600	605	
60	gag gtg gct gcc agc tct ggg ccc cca acc ctc acc agc ctc aac atc	1872		
	Glu Val Ala Ala Ser Ser Gly Pro Pro Thr Leu Thr Ser Leu Asn Ile			
	610	615	620	
	cca ccc ggg ccc tac agc tcc atg cac aag ctg ctg gag aca cag agt	1920		
	Pro Pro Gly Pro Tyr Ser Ser Met His Lys Leu Leu Glu Thr Gln Ser			
	625	630	635	640

	aca ggt gcc tgc caa agc tct tgc aag atc tcc agc cct tgc ttg aaa Thr Gly Ala Cys Gln Ser Ser Cys Lys Ile Ser Ser Pro Cys Leu Lys 645 650 655	1968
5	gca gac agt gga gcc tgt ggt cca gac agc tgc ccc tac tgt gcc cgg Ala Asp Ser Gly Ala Cys Gly Pro Asp Ser Cys Pro Tyr Cys Ala Arg 660 665 670	2016
10	gcc ggg gca ggg gag gtg gag ctc gcc gac cgt gaa atg cct gac tca Ala Gly Ala Gly Glu Val Glu Leu Ala Asp Arg Glu Met Pro Asp Ser 675 680 685	2064
15	gac agc gag gca gtt tat gag ttc aca cag gat gcc cag cac agc gac Asp Ser Glu Ala Val Tyr Glu Phe Thr Gln Asp Ala Gln His Ser Asp 690 695 700	2112
20	ctc cgg gac ccc cac agc cgg cgg caa cgg agc ctg ggc cca gat gca Leu Arg Asp Pro His Ser Arg Arg Gln Arg Ser Leu Gly Pro Asp Ala 705 710 715 720	2160
	gag ccc agc tct gtg ctg gcc ttc tgg agg cta atc tgt gac acc ttc Glu Pro Ser Ser Val Leu Ala Phe Trp Arg Leu Ile Cys Asp Thr Phe 725 730 735	2208
25	cga aag att gtg gac agc aag tac ttt ggc cgg gga atc atg atc gcc Arg Lys Ile Val Asp Ser Lys Tyr Phe Gly Arg Gly Ile Met Ile Ala 740 745 750	2256
30	atc ctg gtc aac aca ctc agc atg ggc atc gaa tac cac gag cag ccc Ile Leu Val Asn Thr Leu Ser Met Gly Ile Glu Tyr His Glu Gln Pro 755 760 765	2304
35	gag gag ctt acc aac gcc cta gaa atc agc aac atc gtc ttc acc agc Glu Glu Leu Thr Asn Ala Leu Glu Ile Ser Asn Ile Val Phe Thr Ser 770 775 780	2352
40	ctc ttt gcc ctg gag atg ctg ctg aag ctg ctt gtg tat ggt ccc ttt Leu Phe Ala Leu Glu Met Leu Leu Lys Leu Val Tyr Gly Pro Phe 785 790 795 800	2400
	ggc tac atc aag aat ccc tac aac atc ttc gat ggt gtc att gtg gtc Gly Tyr Ile Lys Asn Pro Tyr Asn Ile Phe Asp Gly Val Ile Val Val 805 810 815	2448
45	atc agc gtg tgg gag atc gtg ggc cag cag ggg ggc ggc ctg tcg gtg Ile Ser Val Trp Glu Ile Val Gly Gln Gln Gly Gly Leu Ser Val 820 825 830	2496
50	ctg cgg acc ttc cgc ctg atg cgt gtg ctg aag ctg gtg cgc ttc ctg Leu Arg Thr Phe Arg Leu Met Arg Val Leu Lys Leu Val Arg Phe Leu 835 840 845	2544
55	ccg gcg ctg cag cgg cag ctg gtg gtg ctc atg aag acc atg gac aac Pro Ala Leu Gln Arg Gln Leu Val Val Leu Met Lys Thr Met Asp Asn 850 855 860	2592
	gtg gcc acc ttc tgc atg ctg ctt atg ctc ttc atc ttc atc ttc agc Val Ala Thr Phe Cys Met Leu Leu Met Leu Phe Ile Phe Ile Phe Ser 865 870 875 880	2640
60	atc ctg ggc atg cat ctc ttc ggc tgc aag ttt gcc tct gag cgg gat Ile Leu Gly Met His Leu Phe Gly Cys Lys Phe Ala Ser Glu Arg Asp 885 890 895	2688

	ggg gac acc ctg cca gac cgg aag aat ttt gac tcc ttg ctc tgg gcc	2736	
Gly Asp Thr Leu Pro Asp Arg Lys Asn Phe Asp Ser Leu Leu Trp Ala			
900	905	910	
5	atc gtc act gtc ttt cag atc ctg acc cag gag gac tgg aac aaa gtc	2784	
Ile Val Thr Val Phe Gln Ile Leu Thr Gln Glu Asp Trp Asn Lys Val			
915	920	925	
10	ctc tac aat ggt atg gcc tcc acg tcg tcc tgg gcg gcc ctt tat ttc	2832	
Leu Tyr Asn Gly Met Ala Ser Thr Ser Ser Trp Ala Ala Leu Tyr Phe			
930	935	940	
15	att gcc ctc atg acc ttc ggc aac tac gtg ctc ttc aat ttg ctg gtc	2880	
Ile Ala Leu Met Thr Phe Gly Asn Tyr Val Leu Phe Asn Leu Leu Val			
945	950	955	960
20	gcc att ctg gtg gag ggc ttc cag gcg gag gga gat gcc aac aag tcc	2928	
Ala Ile Leu Val Glu Gly Phe Gln Ala Glu Gly Asp Ala Asn Lys Ser			
965	970	975	
25	gaa tca gag ccc gat ttc ttc tca ccc agc ctg gat ggt gat ggg gac	2976	
Glu Ser Glu Pro Asp Phe Ser Pro Ser Leu Asp Gly Asp Gly Asp			
980	985	990	
30	agg aag aag tgc ttg gcc ttg gtg tcc ctg gga gag cac ccg gag ctg	3024	
Arg Lys Lys Cys Leu Ala Leu Val Ser Leu Gly Glu His Pro Glu Leu			
995	1000	1005	
35	atg tcg ctg ccc aag agc acc acg ggc ctg ggc gag gcg ctg ggc	3120	
Met Ser Leu Pro Lys Ser Thr Ser Thr Gly Leu Gly Glu Ala Leu Gly			
1025	1030	1035	1040
40	cct gcg tcg cgc cgc acc agc agc agc ggg tcg gca gag cct ggg gcg	3168	
Pro Ala Ser Arg Arg Thr Ser Ser Gly Ser Ala Glu Pro Gly Ala			
1045	1050	1055	
45	gcc cac gag atg aag tca ccg ccc agc gcc cgc agc tct ccg cac agc	3216	
Ala His Glu Met Lys Ser Pro Pro Ser Ala Arg Ser Ser Pro His Ser			
1060	1065	1070	
50	ccc tgg agc gct gca agc agc tgg acc agc agg cgc tcc agc cgg aac	3264	
Pro Trp Ser Ala Ala Ser Ser Trp Thr Ser Arg Arg Ser Ser Arg Asn			
1075	1080	1085	
55	agc ctc ggc cgt gca ccc agc ctg aag cgg aga agc cca agt gga gag	3312	
Ser Leu Gly Arg Ala Pro Ser Leu Lys Arg Arg Ser Pro Ser Gly Glu			
1090	1095	1100	
60	cgg cgg tcc ctg ttg tcg gga gaa ggc cag gag agc cag gat gaa gag	3360	
Arg Arg Ser Leu Leu Ser Gly Glu Gly Gln Glu Ser Gln Asp Glu Glu			
1105	1110	1115	1120
gag agc tca gaa gag gag cgg gcc agc cct gcg ggc agt gac cat cgc	3406		
Glu Ser Ser Glu Glu Glu Arg Ala Ser Pro Ala Gly Ser Asp His Arg			
1125	1130	1135	
cac agg ggg tcc ctg gag cgg gag gcc aag agt tcc ttt gac ctg cca	3456		
His Arg Gly Ser Leu Glu Arg Glu Ala Lys Ser Ser Phe Asp Leu Pro			
1140	1145	1150	

gac aca ctg cag gtg cca ggg ctg cat cgc act gcc aat ggc cga ggg Asp Thr Leu Gln Val Pro Gly Leu His Arg Thr Ala Ser Gly Arg Gly 1155 1160 1165	3504
5	
tct gct tct gag cac cag gac tgc aat ggc aag tcg gct tca ggg cgc Ser Ala Ser Glu His Gln Asp Cys Asn Gly Lys Ser Ala Ser Gly Arg 1170 1175 1180	3552
10	
ctg gcc cgg gcc ctg cgg cct gat gac ccc cca ctg gat ggg gat gac Leu Ala Arg Ala Leu Arg Pro Asp Asp Pro Pro Leu Asp Gly Asp Asp 1185 1190 1195 1200	3600
15	
gcc gat gac gag ggc aac ctg agc aaa ggg gaa cgg gtc cgc gcg tgg Ala Asp Asp Glu Gly Asn Leu Ser Lys Gly Glu Arg Val Arg Ala Trp 1205 1210 1215	3648
20	
atc cga gcc cga ctc cct gcc tgc tgc ctc gag cga gac tcc tgg tca Ile Arg Ala Arg Leu Pro Ala Cys Cys Leu Glu Arg Asp Ser Trp Ser 1220 1225 1230	3696
25	
gcc tac atc ttc cct cct cag tcc agg ttc cgc ctc ctg tgt cac cgg Ala Tyr Ile Phe Pro Pro Gln Ser Arg Phe Arg Leu Leu Cys His Arg 1235 1240 1245	3744
30	
atc atc acc cac aag atg ttc gac cac gtg gtc ctt gtc atc atc ttc Ile Ile Thr His Lys Met Phe Asp His Val Val Leu Val Ile Ile Phe 1250 1255 1260	3792
35	
ctt aac tgc atc acc atc gcc atg gag cgc ccc aaa att gac ccc cac Leu Asn Cys Ile Thr Ile Ala Met Glu Arg Pro Lys Ile Asp Pro His 1265 1270 1275 1280	3840
40	
agc gct gaa cgc atc ttc ctg acc ctc tcc aat tac atc ttc acc gca Ser Ala Glu Arg Ile Phe Leu Thr Leu Ser Asn Tyr Ile Phe Thr Ala 1285 1290 1295	3888
45	
gtc ttt ctg gct gaa atg aca gtg aag gtg gtg gca ctg ggc tgg tgc Val Phe Leu Ala Glu Met Thr Val Lys Val Val Ala Leu Gly Trp Cys 1300 1305 1310	3936
50	
ttc ggg gag cag gcg tac ctg cgg agc agt tgg aac gtg ctg gac ggg Phe Gly Glu Gln Ala Tyr Leu Arg Ser Ser Trp Asn Val Leu Asp Gly 1315 1320 1325	3984
55	
ctg ttg gtg ctc atc tcc gtc atc gac att ctg gtg tcc atg gtc tct Leu Leu Val Leu Ile Ser Val Ile Asp Ile Leu Val Ser Met Val Ser 1330 1335 1340	4032
60	
gac agc ggc acc aag atc ctg ggc atg ctg agg gtg ctg cgg ctg ctg Asp Ser Gly Thr Lys Ile Leu Gly Met Leu Arg Val Leu Arg Leu Leu 1345 1350 1355 1360	4080
65	
cgg acc ctg cgc ccg ctc agg gtg atc agc cgg gcg cag ggg ctg aag Arg Thr Leu Arg Pro Leu Arg Val Ile Ser Arg Ala Gln Gly Leu Lys 1365 1370 1375	4128
70	
ctg gtg gtg gag acg ctg atg tcc tca ctg aaa ccc atc ggc aac att Leu Val Val Glu Thr Leu Met Ser Ser Leu Lys Pro Ile Gly Asn Ile 1380 1385 1390	4176
75	
gta gtc atc tgc tgt gcc ttc ttc atc att ttc ggc atc ttg ggg gtg Val Val Ile Cys Cys Ala Phe Phe Ile Ile Phe Gly Ile Leu Gly Val 1395 1400 1405	4224

	cag ctc ttc aaa ggg aag ttt ttc gtg tgc cag ggc gag gat acc agg	4272
	Gln Leu Phe Lys Gly Lys Phe Phe Val Cys Gln Gly Glu Asp Thr Arg	
5	1410 1415 1420	
	aac atc acc aat aaa tcg gac tgt gcc gag gcc agt tac cgg tgg gtc	4320
	Asn Ile Thr Asn Lys Ser Asp Cys Ala Glu Ala Ser Tyr Arg Trp Val	
	1425 1430 1435 1440	
10	cgg cac aag tac aac ttt gac aac ctt ggc cag gcc ctg atg tcc ctg	4363
	Arg His Lys Tyr Asn Phe Asp Asn Leu Gly Gln Ala Leu Met Ser Leu	
	1445 1450 1455	
15	ttc gti ttg gcc tcc aag gat ggt tgg gtg gac atc atg tac gat ggg	4416
	Phe Val Leu Ala Ser Lys Asp Gly Trp Val Asp Ile Met Tyr Asp Gly	
	1460 1465 1470	
20	ctg gat gct gtg ggc gtg gac cag cag ccc atc atg aac cac aac ccc	4464
	Leu Asp Ala Val Gly Val Asp Gln Gln Pro Ile Met Asn His Asn Pro	
	1475 1480 1485	
	tgg atg ctg ctg tac ttc atc tcg ttc ctg ctc att gtg gcc ttc ttt	4512
	Trp Met Leu Leu Tyr Phe Ile Ser Phe Leu Leu Ile Val Ala Phe Phe	
	1490 1495 1500	
25	gtc ctg aac atg ttt gtg ggt gtg gtg gaa aac ttc cac aag ttt	4560
	Val Leu Asn Met Phe Val Gly Val Val Val Glu Asn Phe His Lys Cys	
	1505 1510 1515 1520	
30	cgg cag cac cag gag gaa gag gag gcc cgg cgg gag gag aag cgc	4608
	Arg Gln His Gln Glu Glu Glu Ala Arg Arg Arg Glu Glu Lys Arg	
	1525 1530 1535	
35	cta cga aga ctg gag aaa aag aga agg agt aag gag aag cag atg gct	4656
	Leu Arg Arg Leu Glu Lys Lys Arg Arg Ser Lys Glu Lys Gln Met Ala	
	1540 1545 1550	
40	gat cta atg ctg gac gat gta att gct tcc ggc agc tca gcc agc gct	4704
	Asp Leu Met Leu Asp Asp Val Ile Ala Ser Gly Ser Ser Ala Ser Ala	
	1555 1560 1565	
45	gcg tca gaa gcc cag tgc aaa cct tac tac tcc gac tac tcc cgc ttc	4752
	Ala Ser Glu Ala Gln Cys Lys Pro Tyr Tyr Ser Asp Tyr Ser Arg Phe	
	1570 1575 1580	
50	cgg ctc ctc gtc cac cac ttg tgc acc agc cac tac ctg gac ctc ttc	4800
	Arg Leu Leu Val His His Leu Cys Thr Ser His Tyr Leu Asp Leu Phe	
	1585 1590 1595 1600	
55	atc aca ggt gtc atc ggg ctg aac gtg gtc acc atg gcc atg gag cac	4848
	Ile Thr Gly Val Ile Gly Leu Asn Val Val Thr Met Ala Met Glu His	
	1605 1610 1615	
60	tac cag cag ccc cag att ctg gat gag gct ctg aag atc tgc aac tac	4896
	Tyr Gln Gln Pro Gln Ile Leu Asp Glu Ala Leu Lys Ile Cys Asn Tyr	
	1620 1625 1630	
	atc ttc act gtc atc ttt gtc ttg gag tca gtt ttc aaa ctt gtg gcc	4944
	Ile Phe Thr Val Ile Phe Val Leu Glu Ser Val Phe Lys Leu Val Ala	
	1635 1640 1645	
65	ttt ggt ttc cgt cgg ttc ttc cag gac agg tgg aac cag ctg gac ctg	4992
	Phe Gly Phe Arg Arg Phe Phe Gln Asp Arg Trp Asn Gln Leu Asp Leu	
	1650 1655 1660	

	gcc att gtg ctg ctg tcc atc atg ggc atc acg ctg gag gaa atc gag Ala Ile Val Leu Leu Ser Ile Met Gly Ile Thr Leu Glu Glu Ile Glu 1665 1670 1675 1680	5040
5	gtc aac gcc tcg ctg ccc atc aac ccc acc atc atc cgc atc atg agg Val Asn Ala Ser Leu Pro Ile Asn Pro Thr Ile Ile Arg Ile Met Arg 1685 1690 1695	5088
10	gtg ctg cgc att gcc cga gtg ctg aag ctg ctg aag atg gct gtg ggc Val Leu Arg Ile Ala Arg Val Leu Lys Leu Leu Lys Met Ala Val Gly 1700 1705 1710	5136
15	atg cgg gcg ctg ctg gac acg gtg atg cag gcc ctg ccc cag gtg ggg Met Arg Ala Leu Leu Asp Thr Val Met Gln Ala Leu Pro Gln Val Gly 1715 1720 1725	5184
20	aac ctg gga ctt ctc ttc atg ttg ttg ttc atc ttt gca gct ctg Asn Leu Gly Leu Leu Phe Met Leu Leu Phe Phe Ile Phe Ala Ala Leu 1730 1735 1740	5232
25	ggc gtg gag ctc ttt gga gac ctg gag tgt gac gag aca cac ccc tgt Gly Val Glu Leu Phe Gly Asp Leu Glu Cys Asp Glu Thr His Pro Cys 1745 1750 1755 1760	5280
30	gag ggc ctg ggc cgt cat gcc acc ttt cgg aac ttt ggc atg gcc ttc Glu Gly Leu Gly Arg His Ala Thr Phe Arg Asn Phe Gly Met Ala Phe 1765 1770 1775	5328
35	cta acc ctc ttc cga gtc tcc aca ggt gac aat tgg aat ggc att atg Leu Thr Leu Phe Arg Val Ser Thr Gly Asp Asn Trp Asn Gly Ile Met 1780 1785 1790	5376
40	aag gac acc ctc cgg gac tgt gac cag gag tcc acc tgc tac aac acg Lys Asp Thr Leu Arg Asp Cys Asp Gln Glu Ser Thr Cys Tyr Asn Thr 1795 1800 1805	5424
45	gtc atc tcg cct atc tac ttt gtg tcc ttc gtg ctg acg gcc cag ttc Val Ile Ser Pro Ile Tyr Phe Val Ser Phe Val Leu Thr Ala Gln Phe 1810 1815 1820	5472
50	gtg cta gtc aac gtg gtg atc gcc gtg ctg atg aag cac ctg gag gag Val Leu Val Asn Val Val Ile Ala Val Leu Met Lys His Leu Glu Glu 1825 1830 1835 1840	5520
55	agc aac aag gag gcc aag gag gag gcc gag cta gag gct gag ctg gag Ser Asn Lys Glu Ala Lys Glu Ala Glu Leu Glu Ala Glu Leu Glu 1845 1850 1855	5568
60	ctg gag atg aag acc ctc agc ccc cag ccc cac tcg cca ctg ggc agc Leu Glu Met Lys Thr Leu Ser Pro Gln Pro His Ser Pro Leu Gly Ser 1860 1865 1870	5616
	ccc ttc ctc tgg cct ggg gtc gag ggc ccc gac agc ccc gac agc ccc Pro Phe Leu Trp Pro Gly Val Glu Gly Pro Asp Ser Pro Asp Ser Pro 1875 1880 1885	5664
	aag cct ggg gct ctg cac cca gcg gcc cac gcg aga tca gcc tcc cac Lys Pro Gly Ala Leu His Pro Ala Ala His Aia Arg Ser Ala Ser His 1890 1895 1900	5712
	ttt tcc ctg gag cac ccc acg atg cag ccc cac ccc acg gag ctg cca Phe Ser Leu Glu His Pro Thr Met Gln Pro His Pro Thr Glu Leu Pro 1905 1910 1915 1920	5760

	gga cca gac tta ctg act gtg cggtt aag tct ggg gtc agc cga acg cac Gly Pro Asp Leu Leu Thr Val Arg Lys Ser Gly Val Ser Arg Thr His 1925 1930 1935	5808
5	tct ctg ccc aat gac aac tac atg tgt cggtt cat ggg agc act gcc gag Ser Leu Pro Asn Asp Ser Tyr Met Cys Arg His Gly Ser Thr Ala Glu 1940 1945 1950	5856
10	ggg ccc ctg gga cac agg ggc tgg ggg ctc ccc aaa gct cag tca ggc Gly Pro Leu Gly His Arg Gly Trp Gly Leu Pro Lys Ala Gln Ser Gly 1955 1960 1965	5904
15	tcc gtc ttg tcc gtt cac tcc cag cca gca gat acc agc tac atc ctg Ser Val Leu Ser Val His Ser Gln Pro Ala Asp Thr Ser Tyr Ile Leu 1970 1975 1980	5952
20	cag ctt ccc aaa gat gca cct cat ctg ctc cag ccc cac agc gcc cca Gln Leu Pro Lys Asp Ala Pro His Leu Leu Gln Pro His Ser Ala Pro 1985 1990 1995 2000	6000
	acc tgg ggc acc atc ccc aaa ctg ccc cca cca gga cgc tcc cct ttg Thr Trp Gly Thr Ile Pro Lys Leu Pro Pro Gly Arg Ser Pro Leu 2005 2010 2015	6048
25	gct cag agg cca ctc agg cgc cag gca gca ata agg act gac tcc ttg Ala Gln Arg Pro Leu Arg Arg Gln Ala Ala Ile Arg Thr Asp Ser Leu 2020 2025 2030	6096
30	gac gtt cag ggt ctg ggc agc cgg gaa gac ctg ctg gca gag gtg agt Asp Val Gln Gly Leu Gly Ser Arg Glu Asp Leu Leu Ala Glu Val Ser 2035 2040 2045	6144
35	ggg ccc tcc ccg ccc ctg gcc cgg tac tct ttc tgg ggc cag tca Gly Pro Ser Pro Leu Ala Arg Ala Tyr Ser Phe Trp Gly Gln Ser 2050 2055 2060	6192
40	agt acc cag gca cag cag cac tcc cgc agc cac agc aag atc tcc aag Ser Thr Gln Ala Gln Gln His Ser Arg Ser His Ser Lys Ile Ser Lys 2065 2070 2075 2080	6240
	cac atg acc ccg cca gcc cct tgc cca ggc cca gaa ccc aac tgg ggc His Met Thr Pro Pro Ala Pro Cys Pro Gly Pro Glu Pro Asn Trp Gly 2085 2090 2095	6288
45	aag ggc cct cca gag acc aga agc agc tta gag ttg gac acg gag ctg Lys Gly Pro Pro Glu Thr Arg Ser Ser Leu Glu Leu Asp Thr Glu Leu 2100 2105 2110	6336
50	agc tgg att tca gga gac ctc ctg ccc cct ggc ggc cag gag gag ccc Ser Trp Ile Ser Gly Asp Leu Leu Pro Pro Gly Gly Gln Glu Pro 2115 2120 2125	6384
55	cca tcc cca cgg gac ctg aag aag tgc tac agc gtg gag gcc cag agc Pro Ser Pro Arg Asp Leu Lys Lys Cys Tyr Ser Val Glu Ala Gln Ser 2130 2135 2140	6432
	tgc cag cgc cgg cct acg tcc tgg ctg gat gag cag agg aga cac tct Cys Gln Arg Arg Pro Thr Ser Trp Leu Asp Glu Gln Arg Arg His Ser 2145 2150 2155 2160	6480
60	atc gcc gtc agc tgc ctg gac agc ggc tcc caa ccc cac ctg ggc aca Ile Ala Val Ser Cys Leu Asp Ser Gly Ser Gln Pro His Leu Gly Thr 2165 2170 2175	6528

gac	ccc	tct	aac	ctt	ggg	ggc	cag	cct	ctc	ggg	ggg	cct	ggg	agg	cgg	6576	
Asp	Pro	Ser	Asn	Leu	Gly	Gly	Gln	Pro	Leu	Gly	Gly	Pro	Gly	Ser	Arg		
2180									2185						2190		
5																	
ccc	aag	aaa	aaa	ctc	agc	ccg	cct	agt	atc	acc	ata	gac	ccc	ccc	gag	6624	
Pro	Lys	Lys	Lys	Leu	Ser	Pro	Pro	Ser	Ile	Thr	Ile	Asp	Pro	Pro	Glu		
2195									2200						2205		
10																	
agc	caa	ggt	cct	cg	acc	ccg	ccc	agc	cct	ggt	atc	tgc	ctc	cg	agg	6672	
Ser	Gln	Gly	Pro	Arg	Thr	Pro	Pro	Ser	Pro	Gly	Ile	Cys	Leu	Arg	Arg		
2210									2215						2220		
15																	
agg	gct	ccg	tcc	agc	tcc	aag	gat	ccc	ttg	gcc	tct	ggc	ccc	cct	6720		
Arg	Ala	Pro	Ser	Ser	Asp	Ser	Lys	Asp	Pro	Leu	Ala	Ser	Gly	Pro	Pro		
2225									2230						2235		
20																	
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	Lys Cys Tyr Leu Gly Asp Thr Trp Asn Arg Leu Asp Phe Phe Ile Val	
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	Thr Asn Cys Ser Ala Gly Glu His Asn Pro Phe Lys Gly Ala Ile Asn	
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	ccg gcg ctg cag cgg cag ctg gtg gtg ctc atg aag acc atg gac aac Pro Ala Leu Gln Arg Gln Leu Val Val Leu Met Lys Thr Met Asp Asn 850 855 860	2592
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	ccc cac ccc acg gag ctg cca gga cca gac tta ctg act gtg cggt aag Pro His Pro Thr Glu Leu Pro Gly Pro Asp Leu Leu Thr Val Arg Lys 1890 1895 1900	5712

	tct ggg gtc agc cga acg cac tct ctg ccc aat gac agc tac atg tgt Ser Gly Val Ser Arg Thr His Ser Leu Pro Asn Asp Ser Tyr Met Cys 1905 1910 1915 1920	5760
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10	ctc ccc aaa gct cag tca ggc tcc gtc ttg tcc gtt cac tcc cag cca Leu Pro Lys Ala Gln Ser Gly Ser Val Leu Ser Val His Ser Gln Pro 1940 1945 1950	5856
15	gca gat acc agc tac atc ctg cag ctt ccc aaa gat gca cct cat ctg Ala Asp Thr Ser Tyr Ile Leu Gln Leu Pro Lys Asp Ala Pro His Leu 1955 1960 1965	5904
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	tac agc gtg gag gcc cag agc tgc cag cgc ccg cct acg tcc tgg ctg Tyr Ser Val Glu Ala Gln Ser Cys Gln Arg Arg Pro Thr Ser Trp Leu 2115 2120 2125	6384
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	Pro	Leu	Ala	Ser	Gly	Pro	Pro	Asp	Ser	Met	Ala	Ala	Ser	Pro	Ser	Pro	
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	Lys	Lys	Asp	Val	Leu	Ser	Leu	Ser	Gly	Leu	Ser	Ser	Asp	Pro	Ala	Asp	
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	1					5					10					15	
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	Arg	Ser	Phe	Thr	Gln	Leu	Asn	Asp	Leu	Ser	Gly	Ala	Gly	Gly	Arg	Gln	
	20					25										30	
45	ggg	ccg	ggg	tcg	acg	gaa	aag	gac	ccg	ggc	agc	gcg	gac	tcc	gag	gcg	144
	Gly	Pro	Gly	Ser	Thr	Glu	Lys	Asp	Pro	Gly	Ser	Ala	Asp	Ser	Glu	Ala	
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	Glu	Gly	Leu	Pro	Tyr	Pro	Ala	Leu	Ala	Pro	Val	Val	Phe	Phe	Tyr	Leu	
	50					55										60	
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	Pro	Trp	Phe	Glu	Arg	Val	Ser	Met	Leu	Val	Ile	Leu	Leu	Asn	Cys	Vai	
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	act	ctg	gg	atg	ttc	agg	ccg	tgt	gag	gac	att	gcc	tgt	gac	tcc	cag	336
	Thr	Leu	Gly	Met	Phe	Arg	Pro	Cys	Glu	Asp	Ile	Aia	Cys	Asp	Ser	Gln	
	100					105										110	
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	Arg	Cys	Arg	Ile	Leu	Gln	Ala	Phe	Asp	Asp	Phe	Ile	Phe	Ala	Phe	Phe	

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				960
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				1152

	370	375	380	
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	385 390		395	400
	acc aaa cag cgg gag agt cag ctg atg cgg gag cag cgt gta cga ttc			1248
	Thr Lys Gln Arg Glu Ser Gln Leu Met Arg Glu Gln Arg Val Arg Phe			
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	Leu Ser Asn Ala Ser Thr Leu Ala Ser Phe Ser Glu Pro Gly Ser Cys			
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15	tat gag gag cta ctc aag tac ctg gtg tac atc ctc cga aaa gca gcc			1344
	Tyr Glu Glu Leu Leu Lys Tyr Leu Val Tyr Ile Leu Arg Lys Ala Ala			
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	Arg Arg Leu Ala Gln Val Ser Arg Ala Ile Gly Val Arg Ala Gly Leu			
	450 455		460	
25	ctc agc agc cca gtg gcc cgt agt ggg cag gag ccc cag ccc agt ggc			1440
	Leu Ser Ser Pro Val Ala Arg Ser Gly Gln Glu Pro Gln Pro Ser Gly			
	465 470		475	480
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	Ser Cys Thr Arg Ser His Arg Arg Leu Ser Val His His Leu Val His			
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	His His His His His His Tyr His Leu Gly Asn Gly Thr Leu			
	500 505			510
35	aga gtt ccc cgg gcc agc cca gag atc cag gac agg gat gcc aat ggg			1584
	Arg Val Pro Arg Ala Ser Pro Glu Ile Gln Asp Arg Asp Ala Asn Gly			
	515 520			525
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	Ser Arg Arg Leu Met Leu Pro Pro Pro Ser Thr Pro Thr Pro Ser Gly			
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45	ggc cct ccg agg ggt gcg gag tct gta cac agc ttc tac cat gct gac			1680
	Gly Pro Pro Arg Gly Ala Glu Ser Val His Ser Phe Tyr His Ala Asp			
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	Cys His Leu Glu Pro Val Arg Cys Gln Ala Pro Pro Pro Arg Cys Pro			
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	Ser Glu Ala Ser Gly Arg Thr Val Gly Ser Gly Lys Val Tyr Pro Thr			
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55	gtg cat acc agc cct cca cca gag ata ctg aag gat aaa gca cta gtg			1824
	Val His Thr Ser Pro Pro Glu Ile Leu Lys Asp Lys Ala Leu Val			
	595 600			605
60	gag gtg gcc ccc agc cct ggg ccc acc ctc acc agc ttc aac atc			1872
	Glu Val Ala Pro Ser Pro Gly Pro Pro Thr Leu Thr Ser Phe Asn Ile			
	610 615			620
	cca cct ggg ccc ttc agc tcc atg cac aag ctc ctg gag aca cag agt			1920
	Pro Pro Gly Pro Phe Ser Ser Met His Lys Leu Leu Glu Thr Gln Ser			

	625	630	635	640	
	acg gga gcc tgc cat agc tcc tgc aaa atc tcc agc cct tgc tcc aag Thr Gly Ala Cys His Ser Ser Cys Lys Ile Ser Ser Pro Cys Ser Lys				1963
5		645	650		655
	gca gac agt gga gcc tgc ggg ccg gac agt tgt ccc tac tgt gcc cgg Ala Asp Ser Gly Ala Cys Gly Pro Asp Ser Cys Pro Tyr Cys Ala Arg				2016
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		675	680		685
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20	ctc cgg gat ccc cac agc cgg cgg cga cag cgg agc ctg ggc cca gat Leu Arg Asp Pro His Ser Arg Arg Gln Arg Ser Leu Gly Pro Asp				2160
		705	710		715
	gca gag cct agt tct gtg ctg gct ttc tgg agg ctg atc tgt gac aca Ala Glu Pro Ser Ser Val Leu Ala Phe Trp Arg Leu Ile Cys Asp Thr				2208
25		725	730		735
	ttc cgg aag atc gta gat agc aaa tac ttt ggc cgg gga atc atg atc Phe Arg Lys Ile Val Asp Ser Lys Tyr Phe Gly Arg Gly Ile Met Ile				2256
		740	745		750
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35	ccc gag gag ctc acc aac gcc ctg gaa atc agc aac atc gtc ttc acc Pro Glu Glu Leu Thr Asn Ala Leu Glu Ile Ser Asn Ile Val Phe Thr				2352
		770	775		780
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	ttt ggc tac att aag aat ccc tac aac atc ttt gat ggt gtc att gtg Phe Gly Tyr Ile Lys Asn Pro Tyr Asn Ile Phe Asp Gly Val Ile Val				2448
45		805	810		815
	gtc atc agt gtg tgg gag att gtg ggc cag cag gga ggt ggc ctg tcg Val Ile Ser Val Trp Glu Ile Val Gly Gln Gln Gly Gly Leu Ser				2496
		820	825		830
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		835	840		845
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		850	855		860
60	aac gtg gcc acc ttc tgc atg ctc ctc atg ctg ttc atc ttc atc ttc Asn Val Ala Thr Phe Cys Met Leu Leu Met Leu Phe Ile Phe Ile Phe				2640
		865	870		875
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	gcc atc gtc act gtc ttt cag att ctg act cag gaa gac tgg aat aaz Ala Ile Val Thr Val Phe Gln Ile Leu Thr Gln Glu Asp Trp Asn Lys 915 920 925 2784			
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	1140	1145	1150	
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10	cgg agc tct gcc tct gag cac caa gac tgt aat ggc aag tcg gct tca Arg Ser Ser Ala Ser Glu His Gln Asp Cys Asn Gly Lys Ser Ala Ser 1170 1175 1180			3552
15	ggg cgt ttg gcc cgc acc ctg agg act gat gac ccc caa ctg gat ggg Gly Arg Leu Ala Arg Thr Leu Arg Thr Asp Asp Pro Gln Leu Asp Gly 1185 1190 1195 1200			3600
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40	atc ttc ctc aac tgt atc acc atc gct atg gag cgc ccc aaa att gac Ile Phe Leu Asn Cys Ile Thr Ile Ala Met Glu Arg Pro Lys Ile Asp 1265 1270 1275 1280			3840
45	ccc cac agc gct gag cgc atc ttc ctg acc ctc tcc aac tac atc ttc Pro His Ser Ala Glu Arg Ile Phe Leu Thr Leu Ser Asn Tyr Ile Phe 1285 1290 1295			3888
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	Tyr Val Arg His Lys Tyr Asn Phe Asp Asn Leu Gly Gin Ala Leu Met			
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	Ser Leu Phe Val Leu Ala Ser Lys Asp Gly Trp Val Asp Ile Met Tyr			
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	Asp Gly Leu Asp Ala Val Gly Val Asp Gln Gln Pro Ile Met Asn His			
	1475	1480	1485	
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	Asn Pro Trp Met Leu Leu Tyr Phe Ile Ser Phe Leu Leu Ile Val Ala			
	1490	1495	1500	
	ttc ttt gtc ctg aac atg ttt gtg ggc gtg gtg gtg gag aac ttc cat			4560
	Phe Phe Val Leu Asn Met Phe Val Gly Val Val Val Glu Asn Phe His			
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30	aag tgc aga cag cac cag gag gag gag gag gcg agg cgg cgt gag gag			4608
	Lys Cys Arg Gln His Gln Glu Glu Glu Ala Arg Arg Arg Glu Glu			
	1525	1530	1535	
35	aag cga cta cgg agg ctg gag aaa aag aga agg agt aag gag aag cag			4656
	Lys Arg Leu Arg Arg Leu Glu Lys Lys Arg Arg Ser Lys Glu Lys Gln			
	1540	1545	1550	
40	atg gcc gaa gcc cag tgc aag ccc tac tac tct gac tac tcg aga ttc			4704
	Met Ala Glu Ala Gln Cys Lys Pro Tyr Tyr Ser Asp Tyr Ser Arg Phe			
	1555	1560	1565	
45	cgg ctc ctt gtc cac cac ctg tgt acc agc cac tac ctg gac ctc ttc			4752
	Arg Leu Leu Val His His Leu Cys Thr Ser His Tyr Leu Asp Leu Phe			
	1570	1575	1580	
	atc act ggt gtc atc ggg ctg aac gtg gtc act atg gcc atg gaa cat			4800
	Ile Thr Gly Val Ile Gly Leu Asn Val Val Thr Met Ala Met Glu His			
50	1585	1590	1595	1600
	tac cag ccc cag atc ctg gac gag gct ctg aag atc tgc aat tac			4848
	Tyr Gln Gln Pro Gln Ile Leu Asp Glu Ala Leu Lys Ile Cys Asn Tyr			
	1605	1610	1615	
55	atc ttt acc gtc atc ttt gtc ttt gag tca gtt ttc aaa ctt gtg gcc			4896
	Ile Phe Thr Val Ile Phe Val Phe Glu Ser Val Phe Lys Leu Val Ala			
	1620	1625	1630	
60	ttt ggc ttc cgc cgt ttc cag gac agg tgg aac cag ctg gac ctg			4944
	Phe Gly Phe Arg Arg Phe Phe Gln Asp Arg Trp Asn Gln Leu Asp Leu			
	1635	1640	1645	
	gct att gtg ctt ctg tcc atc atg ggc atc aca ctg gag gag att gag			4992
	Ala Ile Val Leu Leu Ser Ile Met Gly Ile Thr Leu Glu Glu Ile Glu			

	1650	1655	1660	
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5	Val Asn Leu Ser Leu Pro Ile Asn Pro Thr Ile Ile Arg Ile Met Arg			
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	gtg ctc cgc att gct cga gtt ctg aag ctg ttg aag atg gct gtg ggc			5088
	Val Leu Arg Ile Ala Arg Val Leu Lys Leu Leu Lys Met Ala Val Gly			
10	1685	1690	1695	
	atg cgg gca ctg ctg cac acg gtg atg cag gcc ctg ccc cag gtg ggg			5136
	Met Arg Ala Leu Leu His Thr Val Met Gln Ala Leu Pro Gln Val Gly			
	1700	1705	1710	
15	aac ctg gga ctt ctc ttc atg tta ttg ttt ttc atc ttt gca gct ctg			5184
	Asn Leu Gly Leu Leu Phe Met Leu Leu Phe Phe Ile Phe Ala Ala Leu			
	1715	1720	1725	
20	ggc gtg gag ctc ttt gga gac ctg gag tgt gat gag aca cac cct tgt			5232
	Gly Val Glu Leu Phe Gly Asp Leu Glu Cys Asp Glu Thr His Pro Cys			
	1730	1735	1740	
25	gag ggc ttg ggt cgg cat gcc acc ttt agg aac ttt ggt atg gcc ttt			5280
	Glu Gly Leu Gly Arg His Ala Thr Phe Arg Asn Phe Gly Met Ala Phe			
	1745	1750	1755	1760
	ctg acc ctc ttc cga gtc tcc act ggt gac aac tgg aat ggt att atg			5328
	Leu Thr Leu Phe Arg Val Ser Thr Gly Asp Asn Trp Asn Gly Ile Met			
30	1765	1770	1775	
	aag gac acc ctc cgg gac tgt gac cag gag tcc acc tgc tac aac act			5376
	Lys Asp Thr Leu Arg Asp Cys Asp Gln Glu Ser Thr Cys Tyr Asn Thr			
	1780	1785	1790	
35	gtc atc tcc cct atc tac ttt gtg tcc ttc gtg ctg acg gcc cag ttt			5424
	Val Ile Ser Pro Ile Tyr Phe Val Ser Phe Val Leu Thr Ala Gln Phe			
	1795	1800	1805	
40	gtg ctg gtc aac gtg gtc ata gct gtg ctg atg aag cac ctg gaa gaa			5472
	Val Leu Val Asn Val Val Ile Ala Val Leu Met Lys His Leu Glu Glu			
	1810	1815	1820	
45	agc aac aaa gag gcc aag gag gag gcc gag ctc gag gcc gag ctg gag			5520
	Ser Asn Lys Glu Ala Lys Glu Ala Glu Leu Glu Ala Glu Leu Glu			
	1825	1830	1835	1840
	ctg gag atg aag acg ctc agc ccg cag ccc cac tcc ccg ctg ggc agc			5568
	Leu Glu Met Lys Thr Leu Ser Pro Gln Pro His Ser Pro Leu Gly Ser			
50	1845	1850	1855	
	ccc ttc ctc tgg ccc ggg gtg gag ggt gtc aac agt act gac agc cct			5616
	Pro Phe Leu Trp Pro Gly Val Glu Gly Val Asn Ser Thr Asp Ser Pro			
	1860	1865	1870	
55	aag cct ggg gct cca cac acc act gcc cac att gga gca gcc tcg ggc			5664
	Lys Pro Gly Ala Pro His Thr Thr Ala His Ile Gly Ala Ala Ser Gly			
	1875	1880	1885	
60	tcc tcc ctt gag cac ccc acg atg gta ccc cac ccc gag gag gtg cca			5712
	Phe Ser Leu Glu His Pro Thr Met Val Pro His Pro Glu Glu Val Pro			
	1890	1895	1900	
	gtc ccc cta gga cca gac ctg ctg act gtg agg aag tct ggt gtc agc			5760
	Val Pro Leu Gly Pro Asp Leu Leu Thr Val Arg Lys Ser Gly Val Ser			

	1905	1910	1915	1920	
	cgg acg cac tct ctg ccc aat gac agc tac atg tgc cgc aat ggg agc Arg Thr His Ser Leu Pro Asn Asp Ser Tyr Met Cys Arg Asn Gly Ser				5808
5		1925	1930	1935	
	act gct gag aga tcc cta gga cac agg ggc tgg ggg ctc ccc aaa gcc Thr Ala Glu Arg Ser Leu Gly His Arg Gly Trp Gly Leu Pro Lys Ala				5856
	1940	1945		1950	
10	cag tca ggc tcc atc ttg tcc gtt cac tcc caa cca gca gac acc agc Gln Ser Gly Ser Ile Leu Ser Val His Ser Gln Pro Ala Asp Thr Ser				5904
	1955	1960		1965	
15	tgc atc cta cag ctt ccc aaa gat gtg cac tat ctg ctc cag cct cat Cys Ile Leu Gln Leu Pro Lys Asp Val His Tyr Leu Leu Gln Pro His				5952
	1970	1975	1980		
20	ggg gct ccc acc tgg ggc gcc atc cct aaa cta ccc cca cct ggc cgc Gly Ala Pro Thr Trp Gly Ala Ile Pro Lys Leu Pro Pro Pro Gly Arg				6000
	1985	1990	1995	2000	
25	tcc cct ctg gct cag agg cct ctc agg cgc cag gca gca ata agg act Ser Pro Leu Ala Gln Arg Pro Leu Arg Arg Gln Ala Ala Ile Arg Thr				6048
	2005	2010		2015	
	gac tcc ctg gat gtg cag ggc ctg ggt agc cgg gaa gac ctg ttg tca Asp Ser Leu Asp Val Gln Gly Leu Gly Ser Arg Glu Asp Leu Leu Ser				6096
	2020	2025		2030	
30	gag gtg agt ggg ccc tcc tgc cct ctg acc cgg tcc tca tcc ttc tgg Glu Val Ser Gly Pro Ser Cys Pro Leu Thr Arg Ser Ser Ser Phe Trp				6144
	2035	2040	2045		
35	ggc ggg tcg agc atc cag gtg cag cag cgt tcc ggc atc cag agc aaa Gly Gly Ser Ser Ile Gln Val Gln Gln Arg Ser Gly Ile Gln Ser Lys				6192
	2050	2055	2060		
40	gtc tcc aag cac atc cgc ctg cca gcc cct tgc cca ggc ctg gaa ccc Val Ser Lys His Ile Arg Leu Pro Ala Pro Cys Pro Gly Leu Glu Pro				6240
	2065	2070	2075	2080	
45	agc tgg gcc aag gac cct cca gag acc aga agc agc tta gag ctg gac Ser Trp Ala Lys Asp Pro Pro Glu Thr Arg Ser Ser Leu Glu Leu Asp				6288
	2085	2090		2095	
	acg gag ctg agc tgg att tca gga gac ctc ctt ccc agc agc cag gaa Thr Glu Leu Ser Trp Ile Ser Gly Asp Leu Leu Pro Ser Ser Gln Glu				6336
	2100	2105		2110	
50	gaa ccc ctg ttc cca cgg gac ctg aag aag tgc tac agt gta gag acc Glu Pro Leu Phe Pro Arg Asp Leu Lys Lys Cys Tyr Ser Val Glu Thr				6384
	2115	2120		2125	
55	cag agc tgc agg cgc agg cct ggg ttc tgg cta gat gaa cag cgg aga Gln Ser Cys Arg Arg Pro Gly Phe Trp Leu Asp Glu Gln Arg Arg				6432
	2130	2135	2140		
60	cac tcc att gct gtc agc tgt ctg gac agc ggc tcc caa ccc cgc cta His Ser Ile Ala Val Ser Cys Leu Asp Ser Gly Ser Gln Pro Arg Leu				6480
	2145	2150	2155	2160	
	tgt cca agc ccc tca agc ctc ggg ggc caa cct ctt ggg ggt cct ggg Cys Pro Ser Pro Ser Ser Leu Gly Gly Gln Pro Leu Gly Gly Pro Gly				6528

	2165	2170	2175	
	agc cgg cct aag aaa aaa ctc agc cca ccc agt atc tct ata gac ccc Ser Arg Pro Lys Lys Lys Leu Ser Pro Pro Ser Ile Ser Ile Asp Pro			6576
5	2180	2185	2190	
	ccg gag agc cag ggc tct cgg ccc cca tgc agt cct ggt gtc tgc ctc Pro Glu Ser Gln Gly Ser Arg Pro Pro Cys Ser Pro Gly Val Cys Leu			6624
	2195	2200	2205	
10	agg agg agg gcg ccg gcc agt gac tct aag gat ccc tcg gtc tcc agc Arg Arg Arg Ala Pro Ala Ser Asp Ser Lys Asp Pro Ser Val Ser Ser			6672
	2210	2215	2220	
15	ccc ctt gac agc acg gct gcc tca ccc tcc cca aag aaa gac acg ctg Pro Leu Asp Ser Thr Ala Ala Ser Pro Ser Pro Lys Lys Asp Thr Leu			6720
	2225	2230	2235	2240
20	agt ctc tct ggt ttg tct tct gac cca aca gac atg gac ccc Ser Leu Ser Gly Leu Ser Ser Asp Pro Thr Asp Met Asp Pro			6762
	2245	2250		
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	1	5	10	15
	cgt agc ttc acg cag ctc aac gac ctg tcc ggg gcc ggg ggc cgg cag Arg Ser Phe Thr Gln Leu Asn Asp Leu Ser Gly Ala Gly Gly Arg Gln			96
40	20	25	30	
	ggg ccg ggg tcg acg gaa aag gac ccg ggc agc gcg gac tcc gag gcg Gly Pro Gly Ser Thr Glu Lys Asp Pro Gly Ser Ala Asp Ser Glu Ala			144
	35	40	45	
45	gag ggg ctg ccg tac ccg gcg cta gcc ccg gtg gtt ttc ttc tac ttg Glu Gly Leu Pro Tyr Pro Ala Leu Ala Pro Val Val Phe Phe Tyr Leu			192
	50	55	60	
50	agc cag gac agc cgc ccg ccg agc tgg tgt ctc cgc acg gtc tgt aac Ser Gln Asp Ser Arg Pro Arg Ser Trp Cys Leu Arg Thr Val Cys Asn			240
	65	70	75	80
55	ccg tgg ttc gag cga gtc agt atg ctg gtc att ctt ctc aac tgt gtg Pro Trp Phe Glu Arg Val Ser Met Leu Val Ile Leu Leu Asn Cys Val			288
	85	90	95	
60	act ctg ggt atg ttc agg ccg tgt gag gac att gcc tgt gac tcc cag Thr Leu Gly Met Phe Arg Pro Cys Glu Asp Ile Ala Cys Asp Ser Gln			336
	100	105	110	
	cgc tgc cgg atc ctg cag gcc ttc gat gac ttc atc ttt gcc ttc ttt Arg Cys Arg Ile Leu Gln Ala Phe Asp Asp Phe Ile Phe Ala Phe Phe			384
	115	120	125	

	gct gtg gaa atg gtg gtg aag atg gtg gcc ttg ggc atc ttt ggg aag Ala Val Glu Met Val Val Lys Met Val Ala Leu Gly Ile Phe Gly Lys 130 135 140	432
5	aaa tgt tac ctg gga gac act tgg aac cggtt gac ttt ttc att gtc Lys Cys Tyr Leu Gly Asp Thr Trp Asn Arg Leu Asp Phe Phe Ile Val 145 150 155 160	480
10	att gca ggg atg ctg gag tat tcg ctg gac ctg cag aac gtc agc ttc Ile Ala Gly Met Leu Glu Tyr Ser Leu Asp Leu Gln Asn Val Ser Phe 165 170 175	528
15	tcc gca gtc agg aca gtc cgt gtg ctg cga ccg ctc agg gcc att aac Ser Ala Val Arg Thr Val Arg Val Leu Arg Pro Leu Arg Ala Ile Asn 180 185 190	576
20	cgg gtg ccc agc atg cgc att ctc gtc aca tta ctg ctg gac acc ttg Arg Val Pro Ser Met Arg Ile Leu Val Thr Leu Leu Leu Asp Thr Leu 195 200 205	624
25	cct atg ctg ggc aac gtc ctg ctc ttt ttc gtc ttt ttc atc Pro Met Leu Gly Asn Val Leu Leu Leu Cys Phe Phe Val Phe Phe Ile 210 215 220	672
30	ttt ggc atc gtg ggc gtc cag ctg tgg gca gga ctg ctt cgc aac cgg Phe Gly Ile Val Gly Val Gln Leu Trp Ala Gly Leu Leu Arg Asn Arg 225 230 235 240	720
35	tgc ttc ctc ccc gag aac ttc agc ctc ccc ctg agc gtg gac ctg gag Cys Phe Leu Pro Glu Asn Phe Ser Leu Pro Leu Ser Val Asp Leu Glu 245 250 255	768
40	cct tat tac cag aca gag aat gag gac gag agc ccc ttc atc tgc tct Pro Tyr Tyr Gln Thr Glu Asn Glu Asp Glu Ser Pro Phe Ile Cys Ser 260 265 270	816
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55	tat aac agt tcc agc aac acc acc ttt gtc aac tgg aac cag tac tat Tyr Asn Ser Ser Asn Thr Thr Cys Val Asn Trp Asn Gln Tyr Tyr 305 310 315 320	960
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	Phe Met Ile Asn Leu Cys Leu Val Val Ile Ala Thr Gln Phe Ser Glu		
385	390	395	
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	Thr Lys Gln Arg Glu Ser Gln Leu Met Arg Glu Gln Arg Val Arg Phe		
	405	410	415
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	Leu Ser Asn Ala Ser Thr Leu Ala Ser Phe Ser Glu Pro Gly Ser Cys		
	420	425	430
15	tat gag gag cta ctc aag tac ctg gtg tac atc ctc cga aaa gca gcc	1344	
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	435	440	445
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	465	470	475
	480		
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	His His His His His His Tyr His Leu Gly Asn Gly Thr Leu		
	500	505	510
40	aga gtt ccc cg ^g gcc agc cca gag atc cag gac agg gat gcc aat ggg	1584	
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	515	520	525
45	tct cgc cg ^g ctc atg cta cca cca ccc tct aca ccc act ccc tct ggg	1632	
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	Glu Val Ala Pro Ser Pro Gly Pro Pro Thr Leu Thr Ser Phe Asn Ile		
	610	615	620
	625	630	635
	640		

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10	aca gga gca gga gag cca gag tcc gct gac cat gtc atg cct gac tca Thr Gly Ala Gly Glu Pro Glu Ser Ala Asp His Val Met Pro Asp Ser 675 680 685	2064
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	aac gtg gcc acc ttc tgc atg ctc ctc atg ctg ttc atc ttc atc ttc Asn Val Ala Thr Phe Cys Met Leu Leu Met Leu Phe Ile Phe Ile Phe 865 870 875 880	2640
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15	gtc ctc tac aac ggc atg gcc tcc aca tcg tct tgg gct gct ctt tac Val Leu Tyr Asn Gly Met Ala Ser Thr Ser Ser Trp Ala Ala Leu Tyr 930 935 940	2832
20	ttc atc gcc ctc atg act ttt ggc aac tat gtg ctc ttt aac ctg ctg Phe Ile Ala Leu Met Thr Phe Gly Asn Tyr Val Leu Phe Asn Leu Leu 945 950 955 960	2880
25	gtg gcc att ctt gtg gaa gga ttc cag gca gag gga gat gcc acc aag Val Ala Ile Leu Val Glu Gly Phe Gln Ala Glu Gly Asp Ala Thr Lys 965 970 975	2928
30	tct gag tca gag cct gat ttc ttt tcg ccc agt gtg gat ggt gat ggg Ser Glu Ser Glu Pro Asp Phe Phe Ser Pro Ser Val Asp Gly Asp Gly 980 985 990	2976
35	gac aga aag aag cgc ttg gcc ctg gtg gct ttg gga gaa cac gcg gaa Asp Arg Lys Lys Arg Leu Ala Leu Val Ala Leu Gly Glu His Ala Glu 995 1000 1005	3024
40	cta cga aag agc ctt ttg cca ccc ctc atc atc cat acg gct gcg aca Leu Arg Lys Ser Leu Leu Pro Pro Leu Ile Ile His Thr Ala Ala Thr 1010 1015 1020	3072
45	cca atg tca cac ccc aag agc tcc agc aca ggt gtg ggg gaa gca ctg Pro Met Ser His Pro Lys Ser Ser Thr Gly Val Gly Glu Ala Leu 1025 1030 1035 1040	3120
50	ggc tct ggc tct cga cgt acc agt agc agt ggg tcc gct gag cct gga Gly Ser Gly Ser Arg Arg Thr Ser Ser Gly Ser Ala Glu Pro Gly 1045 1050 1055	3168
55	gct gcc cac cat gag atg aaa tgt ccg cca agt gcc cgc agc tcc ccg Ala Ala His His Glu Met Lys Cys Pro Pro Ser Ala Arg Ser Ser Pro 1060 1065 1070	3216
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	agg aac agc ctg ggc cgg gcc ccc agc cta aag cgg agg agc cgg agc Arg Asn Ser Leu Gly Arg Ala Pro Ser Leu Lys Arg Arg Ser Pro Ser 1090 1095 1100	3312
	ggg gag cgg agg tcc ctg ctg tct gga gag ggc cag gag agt cag gat Gly Glu Arg Arg Ser Leu Leu Ser Gly Glu Gly Gln Glu Ser Gln Asp 1105 1110 1115 1120	3360
	gag gag gaa agt tca gaa gag gac cgg gcc agc cca gca ggc agt gac Glu Glu Glu Ser Ser Glu Glu Asp Arg Ala Ser Pro Ala Gly Ser Asp 1125 1130 1135	3408

	cat cgc cac agg ggt tcc ttg gaa cgt gag gcc aag agt tcc ttt gac His Arg His Arg Gly Ser Leu Glu Arg Glu Ala Lys Ser Ser Phe Asp 1140 1145 1150	3456
5	ctg cct gac act ctg cag gtg ccg ggg ctg cac cgc aca gcc agc ggc Leu Pro Asp Thr Leu Gln Val Pro Gly Leu His Arg Thr Ala Ser Gly 1155 1160 1165	3504
10	cgg agc tct gcc tct gag cac caa gac tgt aat ggc aag tcc gct tca Arg Ser Ser Ala Ser Glu His Gln Asp Cys Asn Gly Lys Ser Ala Ser 1170 1175 1180	3552
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30	cac cgg atc atc acc cac aag atg ttt gac cat gtg gtc ctc gtc atc His Arg Ile Ile Thr His Lys Met Phe Asp His Val Val Leu Val Ile 1250 1255 1260	3792
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15	tgg gtc cgg cac aag tac aac ttt gac aac ctg ggc cag gct ctg atg Trp Val Arg His Lys Tyr Asn Phe Asp Asn Leu Gly Gln Aia Leu Met 1445 1450 1455	4368
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25	gat ggg ctg gat gct gtg ggt gtg gat cag cag ccc atc atg aac cac Asp Gly Leu Asp Ala Val Gly Val Asp Gln Gln Pro Ile Met Asn His 1475 1480 1485	4464
30	aac ccc tgg atg ctg cta tac ttc atc tcc ttc ctc atc gtg gcc Asn Pro Trp Met Leu Leu Tyr Phe Ile Ser Phe Leu Leu Ile Val Ala 1490 1495 1500	4512
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	1605 1610 1615	
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15	atg agg gtg ctc cgc att gct cga gtt ctg aag ctg ttg aag atg gct Met Arg Val Leu Arg Ile Ala Arg Val Leu Lys Leu Leu Lys Met Ala 1700 1705 1710	5136
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25	gtg ggg aac ctg gga ctt ctc ttc atg tta ttg ttt ttc atc ttt gca Val Gly Asn Leu Gly Leu Leu Phe Met Leu Leu Phe Phe Ile Phe Ala 1730 1735 1740	5232
30	gct ctg ggc gtg gag ctc ttt gga gac ctg gag tgt gat gag aca cac Ala Leu Gly Val Glu Leu Phe Gly Asp Leu Glu Cys Asp Glu Thr His 1745 1750 1755 1760	5280
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55	cag ttt gtg ctg gtc aac gtg gtc ata gct gtg ctg atg aag cac ctg Gln Phe Val Leu Val Asn Val Val Ile Ala Val Leu Met Lys His Leu 1825 1830 1835 1840	5520
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	ggc agc ccc ttc ctc tgg ccc ggg gtg gag ggt gtc aac agt act gac Gly Ser Pro Phe Leu Trp Pro Gly Val Glu Gly Val Asn Ser Thr Asp 1875 1880 1885	5664
	agc cct aag cct ggg gct cca cac acc act gcc cac att gga gca gcc Ser Pro Lys Pro Gly Ala Pro His Thr Thr Ala His Ile Gly Ala Ala 1890 1895 1900	5712

1905	1910	1915	1920	5760
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5 gtg cca gtc ccc cta gga cca gac ctg ctg act gtg agg aag tct ggt Val Pro Val Pro Leu Gly Pro Asp Leu Leu Thr Val Arg Lys Ser Gly 1925 1930 1935 5808				
10 gtc agc cgg acg cac tct ctg ccc aat gac agc tac atg tgc cgc aat Val Ser Arg Thr His Ser Leu Pro Asn Asp Ser Tyr Met Cys Arg Asn 1940 1945 1950 5856				
15 ggg agc act gct gag aga tcc cta gga cac agg ggc tgg ggg ctc ccc Gly Ser Thr Ala Glu Arg Ser Leu Gly His Arg Gly Trp Gly Leu Pro 1955 1960 1965 5904				
20 aaa gcc cag tca ggc tcc atc ttg tcc gtt cac tcc caa cca gca gac Lys Ala Gln Ser Gly Ser Ile Leu Ser Val His Ser Gln Pro Ala Asp 1970 1975 1980 5952				
25 acc agc tgc atc cta cag ctt ccc aaa gat gtg cac tat ctg ctc cag Thr Ser Cys Ile Leu Gln Leu Pro Lys Asp Val His Tyr Leu Leu Gln 1985 1990 1995 2000 6000				
30 cct cat ggg gct ccc acc tgg ggc gcc atc cct aaa cta ccc cca cct Pro His Gly Ala Pro Thr Trp Gly Ala Ile Pro Lys Leu Pro Pro Pro 2005 2010 2015 6048				
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75 gag acc cag agc tgc agg cgc agg cct ggg ttc tgg cta gat gaa cag Glu Thr Gln Ser Cys Arg Arg Pro Gly Phe Trp Leu Asp Glu Gln 2145 2150 2155 2160 6480				

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 Arg Arg His Ser Ile Ala Val Ser Cys Leu Asp Ser Gly Ser Gln Pro
 2165 2170 2175

5 cg_c ct_a t_t g_t cc_a ag_c cc_c tc_a ag_c ct_c gg_g gg_c ca_a cc_t ct_t gg_g g_t 6576
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 2180 2185 2190

10 cc_t gg_g ag_c cg_g ct_c a_a a_a ct_c ag_c cc_a cc_c ag_t at_c t_c at_a 6624
 Pro Gly Ser Arg Pro Lys Lys Leu Ser Pro Pro Ser Ile Ser Ile
 2195 2200 2205

15 g_a cc_c cc_g ga_g ag_c ca_g gg_c t_c cg_g cc_c ca_a t_g c_c ag_t ct_c gg_t g_c 6672
 Asp Pro Pro Glu Ser Gln Gly Ser Arg Pro Pro Cys Ser Pro Gly Val
 2210 2215 2220

20 tg_c ct_c ag_g ag_g gg_c cc_g ag_t g_a c_t t_c a_a g_a t_t cc_c tc_g gt_c 6720
 Cys Leu Arg Arg Ala Pro Ala Ser Asp Ser Lys Asp Pro Ser Val
 2225 2230 2235 2240

25 t_c cc_a cc_c ct_t g_a c_g ac_c g_t tt_g t_c t_c g_a c_c a_a g_a a_a g_a 6768
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 2245 2250 2255

30 ac_g ct_g ag_t ct_c t_c gg_t tt_g t_c t_c g_a c_c a_a g_a at_g g_a c_c 6816
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 1 5 10 15

50 c_gt ag_c tt_c ac_g ca_g ct_c aa_c g_ac ct_g t_c gg_g gg_c gg_g gg_c cc_g ca_g 96
 Arg Ser Phe Thr Gln Leu Asn Asp Leu Ser Gly Ala Gly Gly Arg Gln
 20 25 30

55 gg_g cc_g gg_g tc_c ac_g g_a a_a g_a c_c gg_g gg_c ag_c g_g g_c g_a t_c g_g g_c 144
 Gly Pro Gly Ser Thr Glu Lys Asp Pro Gly Ser Ala Asp Ser Glu Ala
 35 40 45

60 gag gg_g ct_g cc_g ta_c cc_g g_c cta gg_c cc_g gt_g gtt tt_c tt_c tac tt_g 192
 Glu Gly Leu Pro Tyr Pro Ala Leu Ala Pro Val Val Phe Phe Tyr Leu
 50 55 60

65 ag_c ca_g g_a c_g cc_c gg_g ag_c t_g t_t ct_c cc_g ac_g g_t c_t t_t a_a 240
 Ser Gln Asp Ser Arg Pro Arg Ser Trp Cys Leu Arg Thr Val Cys Asn
 65 70 75 80

70 cc_g tg_g tt_c ga_g g_c a_g t_g ct_g g_t att ct_t ct_c a_a t_t gt_g 288
 Pro Trp Phe Glu Arg Val Ser Met Leu Val Ile Leu Leu Asn Cys Val
 85 90 95

act ct_g gg_t at_g tt_c ag_g gg_c t_t g_a g_a c_t tt_c c_a g 336

	Thr Leu Gly Met Phe Arg Pro Cys Glu Asp Ile Ala Cys Asp Ser Gin			
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5	cgc tgc cgg atc ctg cag gcc ttc gat gac ttc atc ttt gcc ttc ttt	384		
	Arg Cys Arg Ile Leu Gln Ala Phe Asp Asp Phe Ile Phe Ala Phe Phe			
	115	120	125	
10	gct gtg gaa atg gtg gtg aag atg gtg gcc ttg ggc atc ttt ggg aag	432		
	Ala Val Glu Met Val Val Lys Met Val Ala Leu Gly Ile Phe Gly Lys			
	130	135	140	
15	aaa tgt tac ctg gga gac act tgg aac cgg ctt gac ttt ttc att gtc	480		
	Lys Cys Tyr Leu Gly Asp Thr Trp Asn Arg Leu Asp Phe Phe Ile Val			
	145	150	155	160
	att gca ggg atg ctg gag tat tcg ctg gac ctg cag aac gtc agc ttc	528		
	Ile Ala Gly Met Leu Glu Tyr Ser Leu Asp Leu Gln Asn Val Ser Phe			
	165	170	175	
20	tcc gca gtc agg aca gtc cgt gtg ctg cga ccg ctc agg gcc att aac	576		
	Ser Ala Val Arg Thr Val Arg Val Leu Arg Pro Leu Arg Ala Ile Asn			
	180	185	190	
25	cgg gtg ccc agc atg cgc att ctc gtc aca tta ctg ctg gac acc ttg	624		
	Arg Val Pro Ser Met Arg Ile Leu Val Thr Leu Leu Asp Thr Leu			
	195	200	205	
30	cct atg ctg ggc aac gtc ctg ctc tgt ttc ttc gtc ttt ttc atc	672		
	Pro Met Leu Gly Asn Val Leu Leu Leu Cys Phe Phe Val Phe Phe Ile			
	210	215	220	
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	Phe Gly Ile Val Gly Val Gln Leu Trp Ala Gly Leu Leu Arg Asn Arg			
	225	230	235	240
	tgc ttc ctc ccc gag aac ttc agc ctc ccc ctg agc gtg gac ctg gag	768		
	Cys Phe Leu Pro Glu Asn Phe Ser Leu Pro Leu Ser Val Asp Leu Glu			
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	Pro Tyr Tyr Gln Thr Glu Asn Glu Asp Glu Ser Pro Phe Ile Cys Ser			
	260	265	270	
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	Gln Pro Arg Glu Asn Gly Met Arg Ser Cys Arg Ser Val Pro Thr Leu			
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	Arg Gly Glu Gly Gly Gly Pro Pro Cys Ser Leu Asp Tyr Glu Thr			
	290	295	300	
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	Tyr Asn Ser Ser Asn Thr Thr Cys Val Asn Trp Asn Gln Tyr Tyr			
	305	310	315	320
	acc aac tgc tct gcg ggc gag cac aac ccc ttc aaa ggc gcc atc aac	1008		
	Thr Asn Cys Ser Ala Gly Glu His Asn Pro Phe Lys Gly Ala Ile Asn			
	325	330	335	
60	ttt gac aac att ggc tat gcc tgg atc gcc atc ttc cag gtc atc aca	1056		
	Phe Asp Asn Ile Gly Tyr Ala Trp Ile Ala Ile Phe Gln Val Ile Thr			
	340	345	350	
	ctg gag ggc tgg gtc gac atc atg tac ttc gta atg gac gct cac tcc	1104		

	Leu Glu Gly Trp Val Asp Ile Met Tyr Phe Val Met Asp Ala His Ser			
	355	360	365	
5	tic tac aac ttc atc tac ttc att ctt ctc atc atc gtg ggc tcc ttc Phe Tyr Asn Phe Ile Tyr Phe Ile Leu Leu Ile Ile Val Gly Ser Phe		1152	
	370	375	380	
10	ttc atg atc aac ctg tgc ctg gtg att gcc acg cag ttc tcc gag Phe Met Ile Asn Leu Cys Leu Val Val Ile Ala Thr Gln Phe Ser Glu		1200	
	385	390	395	400
	acc aaa cag cgg gag agt cag ctg atg cgg gag cag cgt gta cga ttc Thr Lys Gln Arg Glu Ser Gln Leu Met Arg Glu Gln Arg Val Arg Phe		1248	
	405	410	415	
15	ctg tcc aat gct agc acc ctg gca agc ttc tct gag cca ggc agc tgc Leu Ser Asn Ala Ser Thr Leu Ala Ser Phe Ser Glu Pro Gly Ser Cys		1296	
	420	425	430	
20	tat gag gag cta ctc aag tac ctg gtg tac atc ctc cga aaa gca gcc Tyr Glu Glu Leu Leu Lys Tyr Leu Val Tyr Ile Leu Arg Lys Ala Ala		1344	
	435	440	445	
25	cga agg ctg gcc cag gtc tct agg gct ata ggc gtg cgg gct ggg ctg Arg Arg Leu Ala Gln Val Ser Arg Ala Ile Gly Val Arg Ala Gly Leu		1392	
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	485	490	495	
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	500	505	510	
40	aga gtt ccc cgg gcc agc cca gag atc cag gac agg gat gcc aat ggg Arg Val Pro Arg Ala Ser Pro Glu Ile Gln Asp Arg Asp Ala Asn Gly		1584	
	515	520	525	
45	tct cgc cgg ctc atg cta cca cca ccc tct aca ccc act ccc tct ggg Ser Arg Arg Leu Met Leu Pro Pro Pro Ser Thr Pro Thr Pro Ser Gly		1632	
	530	535	540	
50	ggc cct ccg agg ggt gcg gag tct gta cac agc ttc tac cat gct gac Gly Pro Pro Arg Gly Ala Glu Ser Val His Ser Phe Tyr His Ala Asp		1680	
	545	550	555	560
	tgc cac ttg gag cca gtc cgt tgc cag gca ccc cct ccc aga tgc cca Cys His Leu Glu Pro Val Arg Cys Gln Ala Pro Pro Arg Cys Pro		1728	
	565	570	575	
55	tcg gag gca tct ggt agg act gtg ggt agt ggg aag gtg tac ccc act Ser Glu Ala Ser Gly Arg Thr Val Gly Ser Gly Lys Val Tyr Pro Thr		1776	
	580	585	590	
60	gtg cat acc agc cct cca cca gag ata ctg aag gat aaa gca cta gtg Val His Thr Ser Pro Pro Glu Ile Leu Lys Asp Lys Ala Leu Val		1824	
	595	600	605	
	gag gtg gcc ccc agc cct ggg ccc ccc acc ctc acc agc ttc asc atc		1872	

	Glu Val Ala Pro Ser Pro Gly Pro Pro Thr Leu Thr Ser Phe Asn Ile	
	610 615 620	
5	cca cct ggg ccc ttc agc tcc atg cac aag ctc ctg gag aca cag agt Pro Pro Gly Pro Phe Ser Ser Met His Lys Leu Leu Glu Thr Gln Ser	1920
	625 630 635 640	
10	acg gga gcc tgc cat agc tcc tgc aaa atc tcc agc cct tgc tcc aag Thr Gly Ala Cys His Ser Ser Cys Lys Ile Ser Ser Pro Cys Ser Lys	1968
	645 650 655	
	gca gac agt gga gcc tgc ggg ccg gac agt tgt ccc tac tgt gcc cgg Ala Asp Ser Gly Ala Cys Gly Pro Asp Ser Cys Pro Tyr Cys Ala Arg	2016
	660 665 670	
15	aca gga gca gga gag cca gag tcc gct gac cat gtc atg cct gac tca Thr Gly Ala Gly Pro Glu Ser Ala Asp His Val Met Pro Asp Ser	2064
	675 680 685	
20	gac agc gag gct gtg tat gag ttc aca cag gac gct cag cac agt gac Asp Ser Glu Ala Val Tyr Glu Phe Thr Gln Asp Ala Gln His Ser Asp	2112
	690 695 700	
25	ctc cgg gat ccc cac agc cgg cgg cga cag cgg agc ctg ggc cca gat Leu Arg Asp Pro His Ser Arg Arg Gln Arg Ser Leu Gly Pro Asp	2160
	705 710 715 720	
30	gca gag cct agt tct gtg ctg gct ttc tgg agg ctg atc tgt gac aca Ala Glu Pro Ser Ser Val Leu Ala Phe Trp Arg Leu Ile Cys Asp Thr	2208
	725 730 735	
	tta cgg aag atc gta gat agc aaa tac ttt ggc cgg gga atc atg atc Phe Arg Lys Ile Val Asp Ser Lys Tyr Phe Gly Arg Gly Ile Met Ile	2256
	740 745 750	
35	gcc atc ctg gtc aat aca ctc agc atg ggc atc gag tac cac gag cag Ala Ile Leu Val Asn Thr Leu Ser Met Gly Ile Glu Tyr His Glu Gln	2304
	755 760 765	
40	ccc gag gag ctc acc aac gcc ctg gaa atc agc aac atc gtc ttc acc Pro Glu Glu Leu Thr Asn Ala Leu Glu Ile Ser Asn Ile Val Phe Thr	2352
	770 775 780	
45	agc ctc ttc gcc ttg gag atg ctg ctg aaa ctg ctt gtc tac ggt ccc Ser Leu Phe Ala Leu Glu Met Leu Leu Lys Leu Leu Val Tyr Gly Pro	2400
	785 790 795 800	
50	ttt ggc tac att aag aat ccc tac aac atc ttt gat ggt gtc att gtg Phe Gly Tyr Ile Lys Asn Pro Tyr Asn Ile Phe Asp Gly Val Ile Val	2448
	805 810 815	
	gtc atc agt gtg tgg gag att gtg ggc cag cag gga ggt ggc ctg tcg Val Ile Ser Val Trp Glu Ile Val Gly Gln Gln Gly Gly Leu Ser	2496
	820 825 830	
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	835 840 845	
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	850 855 860	
	aac gtg gcc acc ttc tgc atg ctc ctc atg ctg ttc atc atc ttc	2640

	Asn Val Ala Thr Phe Cys Met Leu Leu Met Leu Phe Ile Phe Ile Phe	
	865 870 875 880	
5	agc atc ctg ggc atg cat ctc ttt ggt tgc aag ttc gca tct gaa cg	2688
	Ser Ile Leu Gly Met His Leu Phe Gly Cys Lys Phe Ala Ser Glu Arg	
	885 890 895	
10	gat ggg gac acg ttg cca gac cg aag aat ttc gac tcc ctg ctc tgg	2736
	Asp Gly Asp Thr Leu Pro Asp Arg Lys Asn Phe Asp Ser Leu Leu Trp	
	900 905 910	
	gcc atc gtc act gtc ttt cag att ctg act cag gaa gac tgg aat aaa	2784
	Ala Ile Val Thr Val Phe Gln Ile Leu Thr Gln Glu Asp Trp Asn Lys	
	915 920 925	
15	gtc ctc tac aac ggc atg gcc tcc aca tcg tct tgg gct gct ctt tac	2832
	Vai Leu Tyr Asn Gly Met Ala Ser Thr Ser Ser Trp Ala Ala Leu Tyr	
	930 935 940	
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	Phe Ile Ala Leu Met Thr Phe Gly Asn Tyr Val Leu Phe Asn Leu Leu	
	945 950 955 960	
25	gtg gcc att ctt gtg gaa gga ttc cag gca gag gga gat gcc acc aag	2928
	Val Ala Ile Leu Val Glu Gly Phe Gin Ala Glu Gly Asp Ala Thr Lys	
	965 970 975	
30	tct gag tca gag cct gat ttc ttt tcg ccc agt gtg gat ggt gat ggg	2976
	Ser Glu Ser Glu Pro Asp Phe Phe Ser Pro Ser Val Asp Gly Asp Gly	
	980 985 990	
	gac aga aag aag cgc ttg gcc ctg gtg gct ttg gga gaa cac gcg gaa	3024
	Asp Arg Lys Lys Arg Leu Ala Leu Val Ala Leu Gly Glu His Ala Glu	
	995 1000 1005	
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	Leu Arg Lys Ser Leu Leu Pro Pro Leu Ile Ile His Thr Ala Ala Thr	
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40	cca atg tca cac ccc aag agc tcc agc aca ggt gtg ggg gaa gca ctg	3120
	Pro Met Ser His Pro Lys Ser Ser Thr Gly Val Gly Glu Ala Leu	
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	Gly Ser Gly Ser Arg Arg Thr Ser Ser Gly Ser Ala Glu Pro Gly	
	1045 1050 1055	
50	gct gcc cac cat gag atg aaa tgt ccg cca agt gcc cgc agc tcc ccg	3216
	Ala Ala His His Glu Met Lys Cys Pro Pro Ser Ala Arg Ser Ser Pro	
	1060 1065 1070	
	cac agt ccc tgg agt gcg gca agc agc tgg acc agc agg cgc tcc agc	3264
	His Ser Pro Trp Ser Ala Ala Ser Ser Trp Thr Ser Arg Arg Ser Ser	
	1075 1080 1085	
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	Arg Asn Ser Leu Gly Arg Ala Pro Ser Leu Lys Arg Arg Ser Pro Ser	
	1090 1095 1100	
60	ggg gag cgg agg tcc ctg ctg tct gga gag ggc cag gag agt cag gat	3360
	Gly Glu Arg Arg Ser Leu Leu Ser Gly Glu Gly Gln Glu Ser Gln Asp	
	1105 1110 1115 1120	
	gag gag gaa agt tca gaa gag gag gac cgg gcc agc cca gca ggc agt gac	3408

	Glu Glu Glu Ser Ser Glu Glu Asp Arg Ala Ser Pro Ala Gly Ser Asp	
	1125 1130 1135	
5	cat cgc cac agg ggt tcc ttg gaa cgt gag gcc aag aat tcc ttt gac His Arg His Arg Gly Ser Leu Glu Arg Glu Ala Lys Ser Ser Phe Asp 1140 1145 1150	3456
10	ctg cct gac act ctg cag gtg ccg ggg ctg cac cgc aca gcc agc ggc Leu Pro Asp Thr Leu Gln Val Pro Gly Leu His Arg Thr Ala Ser Gly 1155 1160 1165	3504
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30	gcc tgg gtc aga tcc cgg ctt cct gcc tgt tgc cga gag cga gat tcc Ala Trp Val Arg Ser Arg Leu Pro Ala Cys Cys Arg Glu Arg Asp Ser 1220 1225 1230	3696
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40	cac cgg atc atc acc cac aag atg ttt gac cat gtg gtc ctc gtc atc His Arg Ile Ile Thr His Lys Met Phe Asp His Val Val Leu Val Ile 1250 1255 1260	3792
45	atc ttc ctc aac tgt atc acc atc gct atg gag cgc ccc aaa att gac Ile Phe Leu Asn Cys Ile Thr Ile Ala Met Glu Arg Pro Lys Ile Asp 1265 1270 1275 1280	3840
50	ccc cac agc gct gag cgc atc ttc ctg acc ctc tcc aac tac atc ttc Pro His Ser Ala Glu Arg Ile Phe Leu Thr Leu Ser Asn Tyr Ile Phe 1285 1290 1295	3888
55	acg gca gtc ttt cta gct gaa atg aca gtg aag gtg gtg gca ctg ggc Thr Ala Val Phe Leu Ala Glu Met Thr Val Lys Val Val Ala Leu Gly 1300 1305 1310	3936
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	Leu Lys Leu Val Val Glu Thr Leu Met Ser Ser Leu Lys Pro Ile Gly		
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	1410 1415 1420		
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15	1425 1430 1435 1440		
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	1445 1450 1455		
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	1460 1465 1470		
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	1475 1480 1485		
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	1490 1495 1500		
	ttc ttt gtc ctg aac atg ttt gtg ggc gtg gtg gat aac ttc cat Phe Phe Val Leu Asn Met Phe Val Gly Val Val Val Glu Asn Phe His		4560
35	1505 1510 1515 1520		
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	1525 1530 1535		
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	1540 1545 1550		
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	1555 1560 1565		
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	1570 1575 1580		
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55	1585 1590 1595 1600		
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	1620 1625 1630		
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	Gln Asp Arg Trp Asn Gln Leu Asp Leu Ala Ile Val Leu Leu Ser Ile			
	1635	1640	1645	
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	ctg aag ctg ttg aag atg gct gtg ggc atg cgg gca ctc ctg cac acg Leu Lys Leu Leu Lys Met Ala Val Gly Met Arg Ala Leu Leu His Thr		5088	
15	1685	1690	1695	
	gtg atg cag gcc ctg ccc cag gtg ggg aac ctg gga ctt ctc ttc atg Val Met Gln Ala Leu Pro Gln Val Gly Asn Leu Gly Leu Leu Phe Met		5136	
	1700	1705	1710	
20	tta ttg ttt ttc atc ttt gca gct ctg ggc gtg gag ctc ttt gga gac Leu Leu Phe Phe Ile Phe Ala Ala Leu Gly Val Glu Leu Phe Gly Asp		5184	
	1715	1720	1725	
25	ctg gag tgt gat gag aca cac cct tgt gag ggc ttg ggt cgg cat gcc Leu Glu Cys Asp Glu Thr His Pro Cys Glu Gly Leu Gly Arg His Ala		5232	
	1730	1735	1740	
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	1745	1750	1755	1760
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35	1765	1770	1775	
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	1795	1800	1805	
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	1825	1830	1835	1840
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55	1845	1850	1855	
	gag ggt gtc aac agt act gac agc cct aag cct ggg gct cca cac acc Glu Gly Val Asn Ser Thr Asp Ser Pro Lys Pro Gly Ala Pro His Thr		5616	
	1860	1865	1870	
60	act gcc cac att gga gca gcc tcg ggc ttc tcc ctt gag cac ccc acg Thr Ala His Ile Gly Ala Ala Ser Gly Phe Ser Leu Glu His Pro Thr		5664	
	1875	1880	1885	
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	Met Val Pro His Pro Glu Glu Val Pro Val Pro Leu Gly Pro Asp Leu	
	1890 1895 1900	
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25	atc cct aaa cta ccc cca cct ggc cgc tcc cct ctg gct cag agg cct Ile Pro Lys Leu Pro Pro Gly Arg Ser Pro Leu Ala Gln Arg Pro 1985 1990 1995 2000	6000
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40	cag cag cgt tcc ggc atc cag agc aaa gtc tcc aag cac atc cgc ctg Gln Gln Arg Ser Gly Ile Gln Ser Lys Val Ser Lys His Ile Arg Leu 2050 2055 2060	6192
45	cca gcc cct tgc cca ggc ctg gaa ccc agc tgg gcc aag gac cct cca Pro Ala Pro Cys Pro Gly Leu Glu Pro Ser Trp Ala Lys Asp Pro Pro 2065 2070 2075 2080	6240
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55	ctg aag aag tgc tac agt gta gag acc cag agc tgc agg cgc agg cct Leu Lys Lys Cys Tyr Ser Val Glu Thr Gln Ser Cys Arg Arg Arg Pro 2115 2120 2125	6384
60	ggg ttc tgg cta gat gaa cag cgg aga cac tcc att gct gtc agc tgt Gly Phe Trp Leu Asp Glu Gln Arg Arg His Ser Ile Ala Val Ser Cys 2130 2135 2140	6432
	ctg gac agc ggc tcc caa ccc cgc cta tgt cca agc ccc tca agc ctc	6480

	Leu Asp Ser Gly Ser Gln Pro Arg Leu Cys Pro Ser Pro Ser Ser Leu		
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5	ggg ggc caa cct ctt ggg ggt cct ggg agc cgg cct aag aaa aaa ctc Gly Gly Gin Pro Leu Gly Gly Pro Gly Ser Arg Pro Lys Lys Lys Leu 2165 2170 2175		6528
10	agc cca ccc agt atc tct ata gac ccc ccg gag agc cag ggc tct cgg Ser Pro Pro Ser Ile Ser Ile Asp Pro Pro Glu Ser Gln Gly Ser Arg 2180 2185 2190		6576
15	ccc cca tgc agt cct ggt gtc tgc ctc agg agg agg gcg ccg gcc agt Pro Pro Cys Ser Pro Gly Val Cys Leu Arg Arg Arg Ala Pro Ala Ser 2195 2200 2205		6624
20	gac tct aag gat ccc tcg gtc tcc agc ccc ctt gac agc acg gct gcc Asp Ser Lys Asp Pro Ser Val Ser Ser Pro Leu Asp Ser Thr Ala Ala 2210 2215 2220		6672
25	tca ccc tcc cca aag aaa gac acg ctg agt ctc tct ggt ttg tct tct Ser Pro Ser Pro Lys Lys Asp Thr Leu Ser Leu Ser Gly Leu Ser Ser 2225 2230 2235 2240		6720
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50	cgg ggc gcc ggg acg cga ggc gga ggg ggg ttc gag ctc ggc gtg tca Arg Gly Ala Gly Thr Arg Gly Gly Gly Phe Glu Leu Gly Val Ser 35 40 45		144
55	ccc tcc gag agc ccg gcg gcc gag cgc tgc gcg gag ctg ggt gcc gac Pro Ser Glu Ser Pro Ala Ala Glu Arg Cys Ala Glu Leu Gly Ala Asp 50 55 60		192
60	gag gag cag cgc gtc ccg tac ccg gcc ttg gcg gcc acg gtc ttc ttc Glu Glu Gln Arg Val Pro Tyr Pro Ala Leu Ala Ala Thr Val Phe Phe 65 70 75 80		240
65	tgc ctc ggt cag acc acg ccg ccg cgc agc tgg tgc ctc cgg ctg gtc Cys Leu Gly Gln Thr Thr Arg Pro Arg Ser Trp Cys Leu Arg Leu Val 85 90 95		288
70	tgc aac cca tgg ttc gag cac gtg agc atg ctg gta atc atg ctc aac Cys Asn Pro Trp Phe Glu His Val Ser Met Leu Val Ile Met Leu Asn		336

	100	105	110	
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5	Cys Val Thr Leu Gly Met Phe Arg Pro Cys Glu Asp Val Glu Cys Gly			
	115	120	125	
	tcc gag cgc tgc aac atc ctg gag gcc ttt gac gcc ttc att ttc gcc			432
	Ser Glu Arg Cys Asn Ile Leu Glu Ala Phe Asp Ala Phe Ile Phe Ala			
	130	135	140	
10	ttt ttt gcg gtg gag atg gtc atc aag atg gtg gcc ttg ggg ctg ttc			480
	Phe Phe Ala Val Glu Met Val Ile Lys Met Val Ala Leu Gly Leu Phe			
	145	150	155	160
15	ggg cag aag tgt tac ctg ggt gac acg tgg aac agg ctg gat ttc ttc			528
	Gly Gln Lys Cys Tyr Leu Gly Asp Thr Trp Asn Arg Leu Asp Phe Phe			
	165	170	175	
20	atc gtc gtg gcg ggc atg atg gag tac tcg ttg gac gga cac aac gtc			576
	Ile Val Val Ala Gly Met Met Glu Tyr Ser Leu Asp Gly His Asn Val			
	180	185	190	
25	agc ctc tcg gct atc agg acc gtc cgg ctg ctg cgg ccc ctc cgc gcc			624
	Ser Leu Ser Ala Ile Arg Thr Val Arg Val Leu Arg Pro Leu Arg Ala			
	195	200	205	
	atc aac cgc gtg cct agc atg cgg atc ctg gtc act ctg ctg ctg gat			672
	Ile Asn Arg Val Pro Ser Met Arg Ile Leu Val Thr Leu Leu Leu Asp			
	210	215	220	
30	acg ctg ccc atg ctc ggg aac gtc ctt ctg ctg tgc ttc ttc gtc ttc			720
	Thr Leu Pro Met Leu Gly Asn Val Leu Leu Leu Cys Phe Phe Val Phe			
	225	230	235	240
35	ttc att ttc ggc atc gtt ggc gtc cag ctc tgg gct ggc ctc ctg cgg			768
	Phe Ile Phe Gly Ile Val Gly Val Gln Leu Trp Ala Gly Leu Leu Arg			
	245	250	255	
40	aac cgc tgc ttc ctg gac agt gcc ttt gtc agg aac aac aac ctg acc			816
	Asn Arg Cys Phe Leu Asp Ser Ala Phe Val Arg Asn Asn Asn Leu Thr			
	260	265	270	
45	ttc ctg cgg ccg tac tac cag acg gag gag ggc gag gag aac ccg ttc			864
	Phe Leu Arg Pro Tyr Tyr Gln Thr Glu Glu Gly Glu Glu Asn Pro Phe			
	275	280	285	
50	atc tgc tcc tca cgc cga gac aac ggc atg cag aag tgc tcg cac atc			912
	Ile Cys Ser Ser Arg Arg Asp Asn Gly Met Gln Lys Cys Ser His Ile			
	290	295	300	
55	ccc ggc cgc cgc gac gtg cgc atg ccc tgc acc ctg ggc tgg gag gcc			960
	Pro Gly Arg Arg Asp Val Arg Met Pro Cys Thr Leu Gly Trp Glu Ala			
	305	310	315	320
60	tac acg cag ccg cag gcc gag ggg gtg ggc gct gca cgc aac gcc tgc			1008
	Tyr Thr Gln Pro Gln Ala Glu Gly Val Gly Ala Ala Arg Asn Ala Cys			
	325	330	335	
	atc aac tgg aac cag tac tac aac gtg tgc cgc tcg ggt gac tcc aac			1056
	Ile Asn Trp Asn Gln Tyr Tyr Asn Val Cys Arg Ser Gly Asp Ser Asn			
	340	345	350	
	ccc cac aac ggt gcc atc aac ttc gac aac acc tgc tac gcc tgg att			1104
	Pro His Asn Gly Ala Ile Asn Phe Asp Asn Thr Cys Tyr Ala Trp Ile			

	355	360	365	
	gcc atc ttc cag gtg atc acg ctg gaa ggc tgg	gtg gac atc atg tac		1152
5	Ala Ile Phe Gln Val Ile Thr Leu Glu Gly Trp	Val Asp Ile Met Tyr		
	370	375	380	
	tac gtc atg gac gcc cac tca ttc tac aac ttc	atc tat ttc atc ctg		1200
	Tyr Val Met Asp Ala His Ser Phe Tyr Asn Phe	Ile Tyr Phe Ile Leu		
	385	390	395	400
10	ctc atc atc gtg ggc tcc ttc atg atc aac ctg	tgc ctg gtg gtg		1248
	Leu Ile Ile Val Gly Ser Phe Phe Met Ile Asn	Leu Cys Leu Val Val		
	405	410	415	
15	att gcc acg cag ttc tcg gag acg aag cag	cgg gag agt cag ctg atg		1296
	Ile Ala Thr Gln Phe Ser Glu Thr Lys Gln Arg	Glu Ser Gln Leu Met		
	420	425	430	
20	cgg gag cag cg ^g gca cgc cac ctg tcc aac	gac acg ctg gcc agc		1344
	Arg Glu Gln Arg Ala Arg His Leu Ser Asn Asp	Ser Thr Leu Ala Ser		
	435	440	445	
25	tcc tcc gag cct ggc agc tgc tac gaa gag	ctg ctg aag tac gtg ggc		1392
	Phe Ser Glu Pro Gly Ser Cys Tyr Glu Glu Leu	Lys Tyr Val Gly		
	450	455	460	
	cac ata ttc cgc aag gtc aag cgg cgc agc	ttg cgc ctc tac gcc cgc		1440
	His Ile Phe Arg Lys Val Lys Arg Arg Ser	Leu Arg Leu Tyr Ala Arg		
	465	470	475	480
30	tgg cag agc cgc tgg cgc aag aag gtg gac	ccc agt gct gtg caa ggc		1488
	Trp Gln Ser Arg Trp Arg Lys Val Asp Pro	Ser Ala Val Gln Gly		
	485	490	495	
35	cag ggt ccc ggg cac cgc cag cgc cgg gca	ggc agg cac aca gca gcc tcg		1536
	Gln Gly Pro Gly His Arg Gln Arg Ala Gly Arg	His Thr Ala Ser		
	500	505	510	
40	gtg cac cac ctg gtc tac cac cac cat cac	cac cac cac cac tac		1584
	Val His His Leu Val Tyr His His His His	Tyr His His His Tyr		
	515	520	525	
45	cat ttc agc cat ggc agc ccc cgc agg ccc	ggc ccc gag cca ggc gcc		1632
	His Phe Ser His Gly Ser Pro Arg Arg Pro	Gly Pro Glu Pro Gly Ala		
	530	535	540	
50	tgc gac acc agg ctg gtc cga gct ggc gcg	ccc ccc tgc cca cct tcc		1680
	Cys Asp Thr Arg Leu Val Arg Ala Gly Ala	Pro Pro Ser Pro Pro Ser		
	545	550	555	560
	cca ggc cgc gga ccc ccc gac gca gag tct	gtg cac agc atc tac cat		1728
	Pro Gly Arg Gly Pro Pro Asp Ala Glu Ser	Val His Ser Ile Tyr His		
	565	570	575	
55	gcc gac tgc cac ata gag ggg ccg cag gag	agg gcc cgg gtg ggc aca		1776
	Ala Asp Cys His Ile Glu Gly Pro Gln Glu Arg	Ala Arg Val Gly Thr		
	580	585	590	
60	tgc cgc agc cac tgc cgc tgc cag cct cag	gct ggc cac agg gct ggg		1824
	Cys Arg Ser His Cys Arg Cys Gln Pro Gln Ala	Gly His Arg Ala Gly		
	595	600	605	
	cac cat gaa cta ccc cac gat cct gcc ctc agg	ggt ggg cag cgg caa		1872
	His His Glu Leu Pro His Asp Pro Ala Leu Arg	Gly Gln Arg Gln		

	610	615	620	
5	agg cag cac cag ccc cg ^g acc ca ^a ggg gaa gt ^g ggc cg ^g tgg acc g ^c c			1920
	Arg Gln His Gln Pro Arg Thr Gln Gly Glu Val Gly Arg Trp Thr Ala			
	625 630 635 640			
	agg cac cg ^g ggg cac gg ^c cc ^g tt ^g ag ^c tt ^g aac ag ^c cc ^t gat cc ^c ta ^c			1968
	Arg His Arg Gly His Gly Pro Leu Ser Leu Asn Ser Pro Asp Pro Tyr			
	645 650 655			
10	gag aag atc cc ^g cat gt ^g gg ^c gag cat gg ^a ct ^g gg ^c ca ^a gg ^c cc ^t			2016
	Glu Lys Ile Pro His Val Ala Gly Glu His Gly Leu Gly Gln Ala Pro			
	660 665 670			
15	gg ^c cat ct ^g tc ^g gg ^c ct ^c ag ^t gt ^g cc ^c tg ^c cc ^c ct ^g cc ^c ag ^c cc ^c cc ^a			2064
	Gly His Leu Ser Gly Leu Ser Val Pro Cys Pro Leu Pro Ser Pro Pro			
	675 680 685			
20	gc ^g gg ^c ac ^a ct ^g ac ^c tg ^t gag ct ^g aag ag ^c tg ^c cc ^g ta ^c tg ^c ac ^c cg ^t			2112
	Ala Gly Thr Leu Thr Cys Glu Leu Lys Ser Cys Pro Tyr Cys Thr Arg			
	690 695 700			
25	gc ^c ct ^g gag gac cc ^g gag gg ^t gag ct ^c ag ^c gg ^c tc ^g gaa ag ^t gg ^a gac			2160
	Ala Leu Glu Asp Pro Glu Gly Glu Leu Ser Gly Ser Glu Ser Gly Asp			
	705 710 715 720			
	tca gat gg ^c cg ^t gg ^c gt ^c tat gaa tt ^c ac ^g ca ^g ga ^c gt ^c cg ^g ca ^c gg ^t			2208
	Ser Asp Gly Arg Gly Val Tyr Glu Phe Thr Gln Asp Val Arg His Gly			
	725 730 735			
30	ga ^c cg ^c tgg gac cc ^c ac ^g cg ^a cc ^a cc ^c cg ^t gc ^g ac ^g ga ^c aca cc ^a gg ^c			2256
	Asp Arg Trp Asp Pro Thr Arg Pro Pro Arg Ala Thr Asp Thr Pro Gly			
	740 745 750			
35	cc ^a gg ^c cc ^a gg ^c ag ^c cc ^c ca ^g cg ^g gg ^a ca ^g ca ^g gg ^a gca gg ^c cc ^g			2304
	Pro Gly Pro Gly Ser Pro Gln Arg Arg Ala Gln Gln Arg Ala Ala Pro			
	755 760 765			
40	gg ^c gag cc ^a gg ^c tgg at ^g gg ^c cg ^c ct ^c tgg gtt acc tt ^c ag ^c gg ^c aag			2352
	Gly Glu Pro Gly Trp Met Gly Arg Leu Trp Val Thr Phe Ser Gly Lys			
	770 775 780			
45	ct ^g cg ^c cg ^c at ^c gt ^g gac ag ^c aag tac tt ^c ag ^c cg ^t gg ^c at ^c at ^g at ^g			2400
	Leu Arg Arg Ile Val Asp Ser Lys Tyr Phe Ser Arg Gly Ile Met Met			
	785 790 795 800			
	gc ^c at ^c ctt gtc aac ac ^g ct ^g ag ^c at ^g gg ^c gt ^g gag tac cat gag ca ^g			2448
	Ala Ile Leu Val Asn Thr Leu Ser Met Gly Val Glu Tyr His Glu Gln			
	805 810 815			
50	cc ^c gag gag ct ^g act aat gct ct ^g gag at ^c ag ^c aac at ^c gt ^g tt ^c acc			2496
	Pro Glu Glu Leu Thr Asn Ala Leu Glu Ile Ser Asn Ile Val Phe Thr			
	820 825 830			
55	ag ^c at ^g ttt gg ^c ct ^g gag at ^g ct ^g aag ct ^g ct ^g gg ^c tc ^g gg ^c cc ^t			2544
	Ser Met Phe Ala Leu Glu Met Leu Leu Lys Leu Leu Ala Cys Gly Pro			
	835 840 845			
60	ct ^g gg ^c tac at ^c cg ^c aac cc ^g tac aac at ^c tt ^c gac gg ^c at ^c at ^c gt ^g			2592
	Leu Gly Tyr Ile Arg Asn Pro Tyr Asn Ile Phe Asp Gly Ile Ile Val			
	850 855 860			
	gt ^c at ^c ag ^c gtc tgg gag at ^c gt ^g gg ^c cag gg ^c gac ggt gg ^c tt ^c tct			2640
	Val Ile Ser Val Trp Glu Ile Val Gly Gln Ala Asp Gly Gly Leu Ser			

865	870	875	880	
gtg ctg cgc acc ttc cgg ctg ctg cgt gtg ctg aag ctg gtg cgc ttt Val Leu Arg Thr Phe Arg Leu Leu Arg Val Leu Lys Leu Val Arg Phe				2688
5	885	890	895	
ctg cca gcc ctg cgg cgc cag ctc gtg gtg ctg gtg aag acc atg gac Leu Pro Ala Leu Arg Arg Gln Leu Val Val Leu Val Lys Thr Met Asp				2736
	900	905	910	
10	aac gtg gct acc ttc tgc acg ctg ctc atg ctc ttc atc ttc atc ttc Asn Val Ala Thr Phe Cys Thr Leu Leu Met Leu Phe Ile Phe Ile Phe			2784
	915	920	925	
15	agc atc ctg ggc atg cac ctt ttc ggc tgc aag ttc agc ctg aag aca Ser Ile Leu Gly Met His Leu Phe Gly Cys Lys Phe Ser Leu Lys Thr			2832
	930	935	940	
20	gac acc gga gac acc gtc cct gac agg aag aac ttc gac tcc ctg ctg Asp Thr Gly Asp Thr Val Pro Asp Arg Lys Asn Phe Asp Ser Leu Leu			2880
	945	950	955	960
25	tgg gcc atc gtc acc gtc ttc cag atc ctg acc cag gag gac tgg aac Trp Ala Ile Val Thr Val Phe Gln Ile Leu Thr Gln Glu Asp Trp Asn			2928
	965	970	975	
30	gtg gtc ctg tac aac ggc atg gcc tcc acc tcc tcc tgg gcc gcc ctc Val Val Leu Tyr Asn Gly Met Ala Ser Thr Ser Ser Trp Ala Ala Leu			2976
	980	985	990	
35	tac ttc gtg gcc ctc atg acc ttc ggc aac tat gtg ctc ttc aac ctg Tyr Phe Val Ala Leu Met Thr Phe Gly Asn Tyr Val Leu Phe Asn Leu			3024
	995	1000	1005	
40	ctg gtg gcc atc ctc gtg gag ggc ttc cag gcg gag ggc gat gcc aac Leu Val Ala Ile Leu Val Glu Gly Phe Gln Ala Glu Gly Asp Ala Asn			3072
	1010	1015	1020	
45	aga tcc gac acg gac gag gac aag acg tcg gtc cac ttc gag gag gac Arg Ser Asp Thr Asp Glu Asp Lys Thr Ser Val His Phe Glu Glu Asp			3120
	1025	1030	1035	1040
50	ttc cac aag ctc aga gaa ctc cag acc aca gag ctg aag atg tgt tcc Phe His Lys Leu Arg Glu Leu Gln Thr Thr Glu Leu Lys Met Cys Ser			3168
	1045	1050	1055	
55	ctg gcc gtg acc ccc aac ggc acc tgg agg gac gag gca gcc tgt ccc Leu Ala Val Thr Pro Asn Gly Thr Trp Arg Asp Glu Ala Ala Cys Pro			3216
	1060	1065	1070	
60	ctc ccc tca tca tgt gca cag ctg cca cgc cca tgc cta ccc cca aga Leu Pro Ser Ser Cys Ala Gln Leu Pro Arg Pro Cys Leu Pro Pro Arg			3264
	1075	1080	1085	
65	gct cac cat tcc tgg atg cag ccc cca gcc tcc cag act ctc ggc gtg Ala His His Ser Trp Met Gln Pro Pro Ala Ser Gln Thr Leu Gly Val			3312
	1090	1095	1100	
70	gca gca gca gct ccg ggg acc cgc cac tgg gag acc aga agc ctc cgg Ala Ala Ala Pro Gly Thr Arg His Trp Glu Thr Arg Ser Leu Arg			3360
	1105	1110	1115	1120
75	cag cct ccg aag ttc tcc ctg tgc ccc ctg ggg ccc agt ggc gcc tgg Gln Pro Pro Lys Phe Ser Leu Cys Pro Leu Gly Pro Ser Gly Ala Trp			3408

	1125	1130	1135	
5	agc agc cgg cgc tcc agc tgg agc agc ctg ggc cgt gcc cag cct caa Ser Ser Arg Arg Ser Ser Trp Ser Ser Leu Gly Arg Ala Gln Pro Gln 1140 1145 1150			3456
10	gcg ccg gcg tgc cag tgt ggg gaa cgt gag tcc ctg ctg tct ggc gag Ala Pro Ala Cys Gln Cys Gly Glu Arg Glu Ser Leu Leu Ser Gly Glu 1155 1160 1165			3504
15	ggc aag ggc agc acc gac gac gaa gct gag gac ggc agg gcg cgc tcc Gly Lys Gly Ser Thr Asp Asp Glu Ala Glu Asp Gly Arg Ala Arg Ser 1170 1175 1180			3552
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25	ccc ctg cgg cgg ccc cct ccc gcc tac caa gtg cgc gat cgc gac ggg Pro Leu Arg Arg Pro Pro Ala Tyr Gln Val Arg Asp Arg Asp Gly 1205 1210 1215			3648
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35	cgt gag gat gca gcc gag ctt gac gac tac tcg gag gac agc tgc tgc Arg Glu Asp Ala Ala Glu Leu Asp Asp Ser Glu Asp Ser Cys Cys 1235 1240 1245			3744
40	ctc cgc ctg cat aaa gtg ctg gtg ccc tac aag ccc cag cgg tgc cgg Leu Arg Leu His Lys Val Leu Val Pro Tyr Lys Pro Gln Arg Cys Arg 1250 1255 1260			3792
45	agc agg agg cct ggg ccc tct acc ctc tac ctc ttc tcc cca cag aac Ser Arg Arg Pro Gly Pro Ser Thr Leu Tyr Leu Phe Ser Pro Gln Asn 1265 1270 1275 1280			3840
50	cgg ttc cgc gtc tcc tgc cag aag gtc atc aca cac aag atg ttt gat Arg Phe Arg Val Ser Cys Gln Lys Val Ile Thr His Lys Met Phe Asp 1285 1290 1295			3888
55	cac gtg gtc ctc gtc ttc atc ttc ctc aac tgc gtc acc atc gcc ctg His Val Val Leu Val Phe Ile Phe Leu Asn Cys Val Thr Ile Ala Leu 1300 1305 1310			3936
60	gag agg cct gac att gat ccc ggc agc acc gag cgg gtc ttc ctc agc Glu Arg Pro Asp Ile Asp Pro Gly Ser Thr Glu Arg Val Phe Leu Ser 1315 1320 1325			3984
65	gtc tcc aat tac atc ttc acg gcc atc ttc gtg gcg gag atg atg gtg Val Ser Asn Tyr Ile Phe Thr Ala Ile Phe Val Ala Glu Met Met Val 1330 1335 1340			4032
70	aag gtg gtg gcc ctg ggg ctg ctg tcc ggc gag cac gcc tac ctg cag Lys Val Val Ala Leu Gly Leu Leu Ser Gly Glu His Ala Tyr Leu Gln 1345 1350 1355 1360			4080
75	agc agc tgg aac ctg ctg gat ggg ctg ctg gtg ctg gtg tcc ctg gtg Ser Ser Trp Asn Leu Leu Asp Gly Leu Leu Val Leu Val Ser Leu Val 1365 1370 1375			4128
80	gac att gtc gtg gcc atg gcc tcg gct ggt ggc gcc aag atc ctg ggt Asp Ile Val Val Ala Met Ala Ser Ala Gly Gly Ala Lys Ile Leu Gly			4176

	1380	1385	1390	
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5	gtt ctg cgc gtg ctg cgt ctg ctg cgg acc ctg cgg cct ctg agg gtc Val Leu Arg Val Leu Arg Leu Leu Arg Thr Leu Arg Pro Leu Arg Val 1395 1400 1405			
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15	tca ctc agg ccc att ggg aac atc gtc ctc atc tgc tgc gcc ttc ttc Ser Leu Arg Pro Ile Gly Asn Ile Val Leu Ile Cys Cys Ala Phe Phe 1425 1430 1435 1440			
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20	atc att ttt ggc att ttg ggt gtg cag ctc ttc aaa ggg aag ttc tac Ile Ile Phe Gly Ile Leu Gly Val Gln Leu Phe Lys Gly Lys Phe Tyr 1445 1450 1455			
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25	tac tgc gag ggc ccc gac acc agg aac atc tcc acc aag gca cag tgc Tyr Cys Glu Gly Pro Asp Thr Arg Asn Ile Ser Thr Lys Ala Gln Cys 1460 1465 1470			
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30	cgg gcc cac tac cgc tgg gtg cga cgc aag tac aac ttc gac aac Arg Ala Ala His Tyr Arg Trp Val Arg Arg Lys Tyr Asn Phe Asp Asn 1475 1480 1485			
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35	ctg ggc cag gcc ctg atg tcg ctg ttc gtg ctg tca tcc aag gat gga Leu Gly Gln Ala Leu Met Ser Leu Phe Val Leu Ser Ser Lys Asp Gly 1490 1495 1500			
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40	tgg gtg aac atc atg tac gac ggg ctg gat gcc gtg ggt gtc gac cag Trp Val Asn Ile Met Tyr Asp Gly Leu Asp Ala Val Gly Val Asp Gln 1505 1510 1515 1520			
				4608
45	cag cct gtg cag aac cac aac ccc tgg atg ctg ctg tac ttc atc tcc Gln Pro Val Gln Asn His Asn Pro Trp Met Leu Leu Tyr Phe Ile Ser 1525 1530 1535			
				4656
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				4704
55	gtg gtc gag aac ttc cac aag tgc cgg ccg cac cag gag gcg gag gag Val Val Glu Asn Phe His Lys Cys Arg Pro His Gln Glu Ala Glu Glu 1555 1560 1565			
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60	gcg cgg cgg cga gag gag aag cgg ctg cgg cgc cta gag agg agg cgc Ala Arg Arg Arg Glu Glu Lys Arg Leu Arg Arg Leu Glu Arg Arg Arg 1570 1575 1580			
				4800
65	agg agc act ttc ccc agc cca gag gcc cag cgc cgg ccc tac tat gcc Arg Ser Thr Phe Pro Ser Pro Glu Ala Gln Arg Arg Pro Tyr Tyr Ala 1585 1590 1595 1600			
				4848
70	gac tac tcg ccc acg cgc cgc tgg att cac tcg ctg tgc acc agc cac Asp Tyr Ser Pro Thr Arg Arg Trp Ile His Ser Leu Cys Thr Ser His 1605 1610 1615			
				4896
75	tat ctc gac ctc ttc atc acc ttc atc atc tgt gtc aac gtc atc acc Tyr Leu Asp Leu Phe Ile Thr Phe Ile Ile Cys Val Asn Val Ile Thr 1620 1625 1630			
				4944

	1635	1640	1645	
	aag tac tgc aac tac gtc ttc acc atc gtg ttt gtc ttc gag gct gca Lys Tyr Cys Asn Tyr Val Phe Thr Ile Val Phe Val Phe Glu Ala Ala			4992
5	1650	1655	1660	
	ctg aag ctg gta gca ttt ggg ttc cgt cgg ttc ttc aag gac agg tgg Leu Lys Leu Val Ala Phe Gly Phe Arg Arg Phe Lys Asp Arg Trp			5040
10	1665	1670	1675	1680
	aac cag ctg gac ctg gcc atc gtg ctg ctg tca ctc atg ggc atc acg Asn Gin Leu Asp Leu Ala Ile Val Leu Leu Ser Leu Met Gly Ile Thr	1685	1690	1695
15	ctg gag gag ata gag atg agc gcc gcg ctg ccc atc aac ccc acc atc Leu Glu Glu Ile Glu Met Ser Ala Ala Leu Pro Ile Asn Pro Thr Ile	1700	1705	1710
20	atc cgc atc atg cgc gtg ctt cgc att gcc cgt gtg ctg aag ctg ctg Ile Arg Ile Met Arg Val Leu Arg Ile Ala Arg Val Leu Lys Leu Leu	1715	1720	1725
25	aag atg gct acg ggc atg cgc gcc ctg ctg gac act gtg gtg caa gct Lys Met Ala Thr Gly Met Arg Ala Leu Leu Asp Thr Val Val Gln Ala	1730	1735	1740
	ctc ccc cag gtg ggg aac ctg ggc ctt ctt ttc atg ctc ctg ttt ttt Leu Pro Gln Val Gly Asn Leu Gly Leu Leu Phe Met Leu Leu Phe Phe	1745	1750	1755
30	atc tat gct gcg ctg gga gtg gag ctg ttc ggg agg ctg gag tgc agt Ile Tyr Ala Ala Leu Gly Val Glu Leu Phe Gly Arg Leu Glu Cys Ser	1765	1770	1775
35	gaa gac aac ccc tgc gag ggc ctg agc agg cac gcc acc ttc agc aac Glu Asp Asn Pro Cys Glu Gly Leu Ser Arg His Ala Thr Phe Ser Asn	1780	1785	1790
40	ttc ggc atg gcc ttc ctc acg ctg ttc cgc gtg tcc acg ggg gac aac Phe Gly Met Ala Phe Leu Thr Leu Phe Arg Val Ser Thr Gly Asp Asn	1795	1800	1805
45	tgg aac ggg atc atg aag gac acg ctg cgc gag tgc tcc cgt gag gac Trp Asn Gly Ile Met Lys Asp Thr Leu Arg Glu Cys Ser Arg Glu Asp	1810	1815	1820
	aag cac tgc ctg agc tac ctg ccg gcc ccg tcg ccc gtc tac ttc gtg Lys His Cys Leu Ser Tyr Leu Pro Ala Pro Ser Pro Val Tyr Phe Val	1825	1830	1835
50	1840			
	acc ttc gtg ctg gtg ccc cag ttc gtg ctg gtg aac gtg gtg gtg gcc Thr Phe Val Leu Val Pro Gln Phe Val Leu Val Asn Val Val Ala	1845	1850	1855
55	gtg ctc atg aag cac ctg gag gag agc aac aag gag gct cgg gag gat Val Leu Met Lys His Leu Glu Glu Ser Asn Lys Glu Ala Arg Glu Asp	1860	1865	1870
60	gcg gag ctg gac gcc gag atc gag ctg gag atg gcg cag ggc ccc ggg Ala Glu Leu Asp Ala Glu Ile Glu Leu Glu Met Ala Gln Gly Pro Gly	1875	1880	1885
	agt gca cgc cgg gtg gac gcg gag agg cct ccc ttg ccc cag gag agt Ser Ala Arg Arg Val Asp Ala Asp Arg Pro Pro Leu Pro Gln Glu Ser			5712

	1890	1895	1900	
	ccg ggc gcc agg gac gcc cca aac ctg gtt gca cgc aag gtg tcc gtg			5760
	Pro Gly Ala Arg Asp Ala Pro Asn Leu Val Ala Arg Lys Val Ser Val			
5	1905	1910	1915	1920
	tcc agg atg ctc tcg ctg ccc aac gac agc tac atg ttc agg ccc gtg			5808
	Ser Arg Met Leu Ser Leu Pro Asn Asp Ser Tyr Met Phe Arg Pro Val			
	1925	1930	1935	
10	gtg cct gcc tcg gcg ccc cac ccc cgc ccc ctg cag gag gtg gag atg			5856
	Val Pro Ala Ser Ala Pro His Pro Arg Pro Leu Gln Glu Val Glu Met			
	1940	1945	1950	
15	gag acc tat ggg gcc ggc acc ccc ttg ggc tcc gtt gcc tct gtg cac			5904
	Glu Thr Tyr Gly Ala Gly Thr Pro Leu Gly Ser Val Ala Ser Val His			
	1955	1960	1965	
20	tct ccg ccc gca gag tcc tgt gcc tcc ctc cag atc cca ctg gct gtg			5952
	Ser Pro Pro Ala Glu Ser Cys Ala Ser Leu Gln Ile Pro Leu Ala Val			
	1970	1975	1980	
25	tcg tcc cca gcc agg agc ggc gag ccc ctc cac gcc ctg tcc cct cgg			6000
	Ser Ser Pro Ala Arg Ser Gly Glu Pro Leu His Ala Leu Ser Pro Arg			
	1985	1990	1995	2000
	ggc aca gcc cgc tcc ccc agt ctc agc cggt ctg ctc tgc aga cag gag			6048
	Gly Thr Ala Arg Ser Pro Ser Leu Ser Arg Leu Leu Cys Arg Gln Glu			
	2005	2010	2015	
30	gct gtg cac acc gat tcc ttg aag gga aga ttg aca gcc cta ggg aca			6096
	Ala Val His Thr Asp Ser Leu Lys Gly Arg Leu Thr Ala Leu Gly Thr			
	2020	2025	2030	
35	ccc tgg atc ctg cag agc ctg gtg aga aaa ccc cgg			6132
	Pro Trp Ile Leu Gln Ser Leu Val Arg Lys Pro Arg			
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	Met Thr Glu Gly Ala Arg Ala Ala Asp Glu Val Arg Val Pro Leu Gly			
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55	cgc cgc ccc tgg ccc tgc ggc gtt ggt ggg ggc gtc ccc gga gag ccc			96
	Arg Arg Pro Trp Pro Cys Gly Val Gly Gly Val Pro Gly Glu Pro			
	20	25	30	
60	cgg ggc gcc ggg acg cga ggc gga ggg ggg ttc gag ctc ggc gtg tca			144
	Arg Gly Ala Gly Thr Arg Gly Gly Gly Phe Glu Leu Gly Val Ser			
	35	40	45	
	ccc tcc gag agc ccg gcg gcc gag cgc tgc gcg gag ctg ggt gcc gac			192
	Pro Ser Glu Ser Pro Ala Ala Glu Arg Cys Ala Glu Leu Gly Ala Asp			
	50	55	60	

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10	tgc aac cca tgg ttc gag cac gtg agc atg ctg gta atc atg ctc aac Cys Asn Pro Trp Phe Glu His Val Ser Met Leu Val Ile Met Leu Asn 100 105 110	336
15	tgc gtg acc ctg ggc atg ttc ccg ccc tgt gag gac ggt gag tgc ggc Cys Val Thr Leu Gly Met Phe Arg Pro Cys Glu Asp Val Glu Cys Gly 115 120 125	384
20	tcc gag cgc tgc aac atc ctg gag gcc ttt gac gcc ttc att ttc gcc Ser Glu Arg Cys Asn Ile Leu Glu Ala Phe Asp Ala Phe Ile Phe Ala 130 135 140	432
25	ttt ttt gcg gtg gag atg gtc atc aag atg gtg gcc ttg ggg ctg ttc Phe Phe Ala Val Glu Met Val Ile Lys Met Val Ala Leu Gly Leu Phe 145 150 155 160	480
30	ggg cag aag tgt tac ctg ggt gac acg tgg aac agg ctg gat ttc ttc Gly Gln Lys Cys Tyr Leu Gly Asp Thr Trp Asn Arg Leu Asp Phe Phe 165 170 175	528
35	atc gtc gtg gcg ggc atg atg gag tac tcg ttg gac gga cac aac gtg Ile Val Val Ala Gly Met Met Glu Tyr Ser Leu Asp Gly His Asn Val 180 185 190	576
40	agc ctc tcg gct atc agg acc gtg ccg gtg ctg cgg ccc ctc cgc gcc Ser Leu Ser Ala Ile Arg Thr Val Arg Val Leu Arg Pro Leu Arg Ala 195 200 205	624
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	ttc ctg cgg ccg tac tac cag acg gag gag ggc gag gag aac ccg ttc Phe Leu Arg Pro Tyr Tyr Gln Thr Glu Glu Gly Glu Glu Asn Pro Phe 275 280 285	864
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	ccc ggc cgc cgc gas gtg cgc atg ccc tgc acc ctg ggc tgg gag gcc Pro Gly Arg Arg Asp Val Arg Met Pro Cys Thr Leu Gly Trp Glu Ala 305 310 315 320	960

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5	atc aac tgg aac cag tac tac aac gtg tgc cgc tcg ggt gac tcc aac Ile Asn Trp Asn Gln Tyr Tyr Asn Val Cys Arg Ser Gly Asp Ser Asn 340 345 350	1056
10	ccc cac aac ggt gcc atc aac ttc gac aac acc tgc tac gcc tgg att Pro His Asn Gly Ala Ile Asn Phe Asp Asn Thr Cys Tyr Ala Trp Ile 355 360 365	1104
15	gcc atc ttc cag gtg atc acg ctg gaa ggc tgg gtg gac atc atg tac Ala Ile Phe Gln Val Ile Thr Leu Glu Gly Trp Val Asp Ile Met Tyr 370 375 380	1152
20	tac gtc atg gac gcc cac tca ttc tac aac ttc atc tat ttc atc ctg Tyr Val Met Asp Ala His Ser Phe Tyr Asn Phe Ile Tyr Phe Ile Leu 385 390 395 400	1200
	ctc atc atc gtg ggc tcc ttc atg atc aac ctg tgc ctg gtg gtg Leu Ile Ile Val Gly Ser Phe Phe Met Ile Asn Leu Cys Leu Val Val 405 410 415	1248
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35	tcc tcc gag cct ggc agc tgc tac gaa gag ctg ctg aag tac gtg ggc Phe Ser Glu Pro Gly Ser Cys Tyr Glu Glu Leu Leu Lys Tyr Val Gly 450 455 460	1392
40	cac ata ttc cgc aag gtc aag cgg cgc agc ttg cgc ctc tac gcc cgc His Ile Phe Arg Lys Val Lys Arg Arg Ser Leu Arg Leu Tyr Ala Arg 465 470 475 480	1440
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10	cac cat gaa cta ccc cac gat cct gcc ctc agg ggt ggg cag cgg caa His His Glu Leu Pro His Asp Pro Ala Leu Arg Gly Gly Gln Arg Gln 610 615 620	1872
15	agg cag cac cag ccc cgg acc caa ggg gaa gtg ggc cgg tgg acc gcc Arg Gln His Gln Pro Arg Thr Gln Gly Glu Val Gly Arg Trp Thr Ala 625 630 635 640	1920
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25	gag aag atc ccg cat gtg gcc ggg gag cat gga ctg ggc caa gcc cct Glu Lys Ile Pro His Val Ala Gly Glu His Gly Leu Gly Gln Ala Pro 660 665 670	2016
30	ggc cat ctg tcg ggc ctc agt gtg ccc tgc ccc ctg ccc agc ccc cca Gly His Leu Ser Gly Leu Ser Val Pro Cys Pro Leu Pro Ser Pro Pro 675 680 685	2064
35	gcg ggc aca ctg acc tgt gag ctg aag agc tgc ccc tac tgc acc cgt Ala Gly Thr Leu Thr Cys Glu Leu Lys Ser Cys Pro Tyr Cys Thr Arg 690 695 700	2112
40	gcc ctg gag gac ccg gag ggt gag ctc agc ggc tcg gaa agt gga gac Ala Leu Glu Asp Pro Glu Gly Glu Leu Ser Gly Ser Glu Ser Gly Asp 705 710 715 720	2160
45	tca gat ggc cgt ggc gtc tat gaa ttc acg cag gac gtc cgg cac ggt Ser Asp Gly Arg Gly Val Tyr Glu Phe Thr Gln Asp Val Arg His Gly 725 730 735	2208
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65	ctg cgc cgc atc gtg gac agc aag tac ttc agc cgt ggc atc atg atg Leu Arg Arg Ile Val Asp Ser Lys Tyr Phe Ser Arg Gly Ile Met Met 785 790 795 800	2400
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	agc atg ttt gcc ctg gag atg ctg ctg aag ctg ctg gcc tgc ggg cct Ser Met Phe Ala Leu Glu Met Leu Leu Lys Leu Leu Ala Cys Gly Pro 835 840 845	2544
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10	gtc atc agc gtc tgg gag atc gtg ggg cag gcg gac ggt ggc ttg tct Val Ile Ser Val Trp Glu Ile Val Gly Gln Ala Asp Gly Gly Leu Ser 865 870 875 880	2640
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	aac gtg gct acc ttc tgc acg ctg ctc atg ctc ttc att ttc atc ttc Asn Val Ala Thr Phe Cys Thr Leu Leu Met Leu Phe Ile Phe Ile Phe 915 920 925	2784
25	agc atc ctg ggc atg cac ctt ttc ggc tgc aag ttc agc ctg aag aca Ser Ile Leu Gly Met His Leu Phe Gly Cys Lys Phe Ser Leu Lys Thr 930 935 940	2832
30	gac acc gga gac acc gtg cct gac agg aag aac ttc gac tcc ctg ctg Asp Thr Gly Asp Thr Val Pro Asp Arg Lys Asn Phe Asp Ser Leu Leu 945 950 955 960	2880
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55	tcc cac aag ctc aga gaa ctc cag acc aca gag ctg aag atg tgt tcc Phe His Lys Leu Arg Glu Leu Gln Thr Thr Glu Leu Lys Met Cys Ser 1045 1050 1055	3168
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	ctc ccc tca tca tgt gca cag ctg cca cgc cca tgc cta ccc cca aga Leu Pro Ser Ser Cys Ala Gln Leu Pro Arg Pro Cys Leu Pro Pro Arg 1075 1080 1085	3264

	gct cac cat tcc tgg atg cag ccc cca gcc tcc cag act ctc ggc gtg Ala His His Ser Trp Met Gln Pro Pro Ala Ser Gln Thr Leu Gly Val 1090 1095 1100	3312
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10	cag cct ccg aag ttc tcc ctg tgc ccc ctg ggg ccc agt ggc gcc tgg Gln Pro Pro Lys Phe Ser Leu Cys Pro Leu Gly Pro Ser Gly Ala Trp 1125 1130 1135	3408
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40	cag gtg gtg gcc ctg ccc agc gac ttc ttc ctg cgc atc gac agc cac Gln Val Val Ala Leu Pro Ser Asp Phe Phe Leu Arg Ile Asp Ser His 1220 1225 1230	3696
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40	cgg gcc gcc cac tac cgc tgg gtg cga cgc aag tac aac ttc gac aac Arg Ala Ala His Tyr Arg Trp Val Arg Arg Lys Tyr Asn Phe Asp Asn 1475 1480 1485	4464
45	ctg ggc cag gcc ctg atg tcg ctg ttc gtg ctg tca tcc aag gat gga Leu Gly Gln Ala Leu Met Ser Leu Phe Val Leu Ser Ser Lys Asp Gly 1490 1495 1500	4512
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	gtg gtc gag aac ttc cac aag tgc cgg ccg cac cag gag gcg gag gag Val Val Glu Asn Phe His Lys Cys Arg Pro His Gln Glu Ala Glu Glu 1555 1560 1565	4704
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15	tcc acc atc gtg ttt gtc ttc gag gct gca ctg aag ctg gta gca ttt Phe Thr Ile Val Phe Val Phe Glu Ala Ala Leu Lys Leu Val Ala Phe 1650 1655 1660	4992
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5	tcc tcc ccg cca ggc ctg gag gag cct ctg gat gga gct gat cct cat Ser Ser Pro Pro Gly Leu Glu Pro Leu Asp Gly Ala Asp Pro His 35	40	45	144
10	gtc cca cac cca gac ctg gcg cct att gcc ttc ttc tgc ctg cga cag Val Pro His Pro Asp Leu Ala Pro Ile Ala Phe Phe Cys Leu Arg Gln 50	55	60	192
15	acc acc agc ccc cgg aac tgg tgc atc aag atg gtg tgc aac ccg tgg Thr Thr Ser Pro Arg Asn Trp Cys Ile Lys Met Val Cys Asn Pro Trp 65	70	75	240
	ttt gaa tgt gtc agc atg ctg gtg atc ctg ctg aac tgc gtg aca ctt Phe Glu Cys Val Ser Met Leu Val Ile Leu Leu Asn Cys Val Thr Leu 85	90	95	288
20	ggc atg tac cag ccg tgc gac gac atg gac tgc ctg tcc gac cgc tgc Gly Met Tyr Gln Pro Cys Asp Asp Met Asp Cys Leu Ser Asp Arg Cys 100	105	110	336
25	aag atc atg cag gtc ttt gat gac ttc atc ttt atc ttc ttt gcc atg Lys Ile Met Gln Val Phe Asp Asp Phe Ile Phe Ile Phe Ala Met 115	120	125	384
30	gag atg gtg ctc aag atg gtg gcc ctg ggg att ttt ggc aag aag tgc Glu Met Val Leu Lys Met Val Ala Leu Gly Ile Phe Gly Lys Lys Cys 130	135	140	432
35	tac ctc ggg gac aca tgg aac cgc ctg gat ttc ttc atc gtc atg gca Tyr Leu Gly Asp Thr Trp Asn Arg Leu Asp Phe Phe Ile Val Met Ala 145	150	155	480
	ggg atg gtc gag tac tcc ctg gac ctt cag aac atc aac ctg tca gcc Gly Met Val Glu Tyr Ser Leu Asp Leu Gln Asn Ile Asn Leu Ser Ala 165	170	175	528
40	atc cgc acc gtg cgc gtc ctg agg ccc ctc aaa gcc atc aac cgc gtc Ile Arg Thr Val Arg Val Leu Arg Pro Leu Lys Ala Ile Asn Arg Val 180	185	190	576
45	ccc agt atg cgg atc ctg gtg aac ctg ctc ctg gac aca ctg ccc atg Pro Ser Met Arg Ile Leu Val Asn Leu Leu Asp Thr Leu Pro Met 195	200	205	624
50	ctg ggg aat gtc ctg ctg tgc ttc ttt gtc ttc ttc atc ttt ggc Leu Gly Asn Val Leu Leu Leu Cys Phe Phe Val Phe Phe Ile Phe Gly 210	215	220	672
55	atc ata ggt gtg cag ctc tgg gcg ggc ctg ctg cgt aac cgc tgc ttc Ile Ile Gly Val Gln Leu Trp Ala Gly Leu Leu Arg Asn Arg Cys Phe 225	230	235	720
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	Gln Gly Arg Glu Cys Cys Leu Ser Lys Asp Asp Val Tyr Asp Phe Gly	
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	Ala Gly Arg Gln Asp Leu Asn Ala Ser Gly Leu Cys Val Asn Trp Asn	
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	Arg Tyr Tyr Asn Val Cys Arg Thr Gly Ser Ala Asn Pro His Lys Gly	
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	Phe Ser Glu Thr Lys Gln Arg Glu His Arg Leu Met Leu Glu Gln Arg	
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	Ala Lys Arg Arg Ala Leu Gly Leu Tyr Gln Ala Leu Gln Ser Arg Arg	
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	Gln Ala Leu Gly Pro Glu Ala Pro Ala Pro Ala Lys Pro Gly Pro His	
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	Ala Lys Glu Pro Arg His Tyr Gln Leu Cys Pro Gln His Ser Pro Leu	
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	Ser Asp Pro Ala Ser Cys Pro Cys Cys Gln His Glu Asp Gly Arg Arg	
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	Ser Ser Glu Asp Gly Ala Ser Ser Glu Leu Gly Lys Glu Glu Glu	
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	Glu Glu Gln Ala Asp Gly Ala Val Trp Leu Cys Gly Asp Val Trp Arg	
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	Glu Thr Arg Ala Lys Leu Arg Gly Ile Val Asp Ser Lys Tyr Phe Asn	
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	cgg ggc atc atg atg gcc atc ctg gtc aac acc gtc agc atg ggc atc	1872
	Arg Gly Ile Met Met Ala Ile Leu Val Asn Thr Val Ser Met Gly Ile	
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25	gag cac cac gag cag ccg gag gag ctg acc aac atc ctg gag atc tgc	1920
	Glu His His Glu Gln Pro Glu Glu Leu Thr Asn Ile Leu Glu Ile Cys	
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30	aat gtg gtc ttc acc agc atg ttt gcc ctg gag atg atc ctg aag ctg	1968
	Asn Val Val Phe Thr Ser Met Phe Ala Leu Glu Met Ile Leu Lys Leu	
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35	gct gca ttt ggg ctc ttc gac tac ctg cgt aac ccc tac aac atc ttc	2016
	Ala Ala Phe Gly Leu Phe Asp Tyr Leu Arg Asn Pro Tyr Asn Ile Phe	
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	gac agc atc att gtc atc atc agc atc tgg gag atc gtg ggg cag gcg	2064
	Asp Ser Ile Ile Val Ile Ser Ile Trp Glu Ile Val Gly Gln Ala	
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	Phe Ser Leu Arg Thr Asp Thr Gly Asp Thr Val Pro Asp Arg Lys Asn	
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	675 680 685	
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	Lys	Met	Ala														

INTERNATIONAL SEARCH REPORT

Intern	al Application No
PCT/US 98/23161	

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/12 C07K14/705 C07K16/28 C12N5/10 G01N33/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 95 04144 A (NEUREX CORP) 9 February 1995	1,2,7, 10-18, 20-22
Y	see abstract; claims 1-10 ---	3,19
X	NOONEY JM (REPRINT) ET AL: "Identifying neuronal non-L Ca ²⁺ channels - more than stamp collecting?" TRENDS IN PHARMACOLOGICAL SCIENCES, 10-1997, 18, 363-371, XP002093637 see page 369, right-hand column - page 370, right-hand column ---	1,2, 10-16, 20-22

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
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"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

16 February 1999

09/03/1999

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Authorized officer

Gurdjian, D

INTERNATIONAL SEARCH REPORT

Intern	nal Application No
PCT/US 98/23161	

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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